CANCER SUPPLEMENT

Through this supplement to the August issue of the Journal of the Kansas Medical Society, the Kansas Division of the American Cancer Society is making available to the physicians of Kansas the papers presented at the Second Annual Mid-West Cancer Conference, last January 19, 20 and 21, as part of its program of professional education.

Every effort has been made to make the publications complete and as valuable as they were when presented at the conference. However, certain obstacles have been insurmountable and the Editorial Board and the Kansas Division of the American Cancer Society regret these shortcomings.

Neither of the papers of Dr. Roy Hertz were available for publication here because they contained material previously promised for publication elsewhere.

In their actual presentations the papers of all the essayists were profusely illustrated with slides (many of them in color) which added greatly to the value of the talks, and would add to the value of the published forms. Duplication of all slides, however, is neither practical nor possible, and as a result the publications of several of the speakers have either been extensively revised or condensed, or they contain references to "slides" which are not reproduced. It is hoped that readers will understand and be tolerant of these deficiencies.

It is the hope of the Kansas Division of the American Cancer Society and of the Editorial Board that this supplement will prove to be interesting and valuable to every physician who has the opportunity to read it.

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Edward Mallinckrodt Professor of Pathology and Dean, Washington University School of Medicine.

Alton Ochsner, M.D., New Orleans, Louisiana

William Henderson Professor of Surgery and Chairman of Department of Surgery, School of Medicine, Tulane University of Louisiana; Director, Section on General Surgery, Ochsner Clinic; Regent, American College of Surgeons; President, American Cancer Society.

PROGRAM

Thursday, January 19, 1950

Afternoon Session

Problems in the Diagnosis of Neoplasms of the Kidney—
R. H. Flocks, M. D. ..... Page 5-A

The Importance of Lymph Node Metastases in Carcinoma of the
Cervix Uteri—A. N. Arneson, M.D. ..... Page 11-A

Malignant Neoplasms of the Skin—Arthur C. Curtis, M.D. ..... Page 13-A

Cancer of the Breast—Herbert Willy Meyer, M.D. ..... Page 18-A

Friday, January 20, 1950

Morning Session

The Use of Hormones in Cancer Therapy—Roy Hertz, M.D.

The Cutaneous Manifestations of Lymphoblastomata—
Arthur C. Curtis, M.D. ..... Page 28-A

The Surgical Treatment of Carcinoma of the Stomach—
W. P. Longmire, Jr., M.D. ..... Page 32-A

The Use of Radium in the Treatment of Endometrial Cancer—
A. N. Arneson, M.D. ..... Page 37-A

PROGRAM

Friday, January 20, 1950

Afternoon Session

Cancer of the Head and Neck Including Cervical Lymph Node Dissections—Herbert Willy Meyer, M.D. ..... Page 39-A

Bronchiogenic Carcinoma—Alton Ochsner, M.D. ..... Page 46-A

Carcinoma of the Bladder with Special Emphasis On Its Surgical Treatment—R. H. Flocks, M.D. ..... Page 50-A

The Present Status of Radiology in the Diagnosis of Curable Cancer—L. H. Garland, M.D. ..... Page 53-A

Dinner Meeting

Progress in the Treatment of Cancer—Alton Ochsner, M.D. ..... Page 56-A

Saturday, January 21, 1950

Morning Session

Malignant Lesions of the Small Intestine—W. P. Longmire, Jr., M.D. ..... Page 59-A

Radiological End Results in the Control of Cancer—L. H. Garland, M.D. ..... Page 63-A

Tumors of the Testis—Robert A. Moore, M.D. ..... Page 70-A

Approaches to the Cancer Problem Through Hormone Studies in Animals—Roy Hertz, M.D.

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Problems in the Diagnosis of Neoplasms of the Kidney

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Neoplasms of the kidney may be divided into three groups. Group A is the Wilms' tumor which occurs primarily in the age group three to eight. Groups B and C are the neoplasms of the adult kidney. Group B are the so-called hypernephroma or tumors arising in the renal substance and Group C are the tumors which arise from the renal pelvis—the papillary carcinoma of the renal pelvis and the squamous cell epithelioma of the renal pelvis. These tumors are relatively infrequent, but not rare. At the University Hospitals, where approximately 80 carcinomas of the bladder are seen in a year, approximately 20 renal tumors occur. Of these, over 90 per cent are tumors of the renal substance and will occur in patients over the age of 30.

It is extremely difficult to make an early diagnosis of these kidney tumors because in the vast majority of instances, no symptoms at all occur until the neoplasm has progressed very significantly. The symptomatology, therefore, may be described as follows: There may be no symptoms and in the large majority of cases, no symptoms are present until the tumor has reached significant size. There may be pain due to the presence of a mass or due to pressure upon adjacent structures or due to the passage of blood clots associated with hematuria. There may be gross hematuria. There may be a mass. There may be fever due to breakdown in the center of the tumor. There may be pains or other symptoms due to metastases or extension of the tumor. Since, in the vast majority of cases, there are no symptoms or one or a combination of the above, one must be continuously on guard in the age group under eight and over 30.

Vague symptoms or other abnormalities may be due to a kidney tumor. Suspicion of the presence of a kidney tumor should be aroused if one of the following is present:

1. an abdominal mass
2. an unexplained fever
3. unexplained chest lesions
4. osteolytic lesion of bone
5. unexplained abdominal pain
6. unexplained loss of weight
7. unexplained anemia
8. any of the signs and symptoms described previously such as pain, hematuria, a mass in the kidney region or unexplained fever.

Since renal neoplasms are only fairly common and since the symptomatology is so variable, the diagnosis depends on one's thinking of it and upon a thorough roentgenological study. Therefore, if any of the above signs or symptoms are present, a thorough roentgenological study should be carried out. This may include the following:

(a) A very careful study is made of the soft tissue outlines of the kidney with special attention being paid to these outlines to see if there is any distortion suggesting the presence of a space-occupying mass in the kidney substance. Calcification in this region is not infrequently present in the presence of hypernephroma. If the soft tissue outline cannot be definitely made out, perirenal oxygen or air injections are frequently of value when one suspects the presence of hypernephroma.

(b) Pyeloureterograms with skiodan and with air frequently are of great value in the diagnosis of hypernephroma or tumor of the kidney pelvis. Distortion of the calices indicates the presence of space-occupying masses in the renal substance. Filling defects may indicate either hypernephroma or papillary tumor of the kidney pelvis. The latter is rarely associated with a change in the renal outline. Blood clots alone or non-opaque calculi must be differentiated if filling defects alone are present. Frequently a lateral pyeloureterogram with skiodan is of value and will show a distortion of the pelvis and calices which cannot be made out by the ordinary anterior-posterior pyeloureterogram.

(c) Occasionally, aortography is of value although this carries hazards which in the vast majority of cases would contraindicate it.

Typical distortion of the renal outline accompanied by distortion of the caliceal system in itself is almost pathognomonic of renal tumor. Differential diagnosis from cyst of the kidney, polycystic disease and renal carbuncle is necessary at times. Ordinarily, polycystic disease is bilateral and, therefore, can easily be differentiated because of associated hypertension and the family history. Solitary cyst is at times very difficult particularly when trying to make a differential diagnosis between cystadenocarcinoma and solitary cyst. Ordinarily, the younger the individual the more likely malignancy is to be present. However, differential diagnosis ordinarily can only be made by removing the kidney and studying it in the laboratory.

In recent years, the urine obtained from the kidney has been studied by the Papanicolaou technique to see if malignant cells can be found which would indicate the presence of renal neoplasm. Extensive studies have been made at the University Hospitals by Doctors R. G. Bunge and Otto Kraushaar. They have found that these studies are of little value thus far in hypernephroma because of the presence, not uncommonly, of false positives. On the other hand, no false positives have thus far been found in papillary tumor of the kidney pelvis. No studies have thus far been made upon Wilms' tumor. However, further studies are being carried out and because of the variability of the symptoms of renal neoplasm and because symptomatology is frequently misleading or does not occur until so very late, there is a real possibility that further advances in these cytological studies will make these studies a valuable adjunct to early diagnosis.

The following case abstracts are illustrative of the above points with regard to the different types of kidney tumor and different situations and problems which may arise with them.

Case I. A two-year-old girl was admitted to the University Hospitals on August 19, 1942. Her parents had noted that the patient's abdomen had been distended for the past year but she had remained in excellent health. Three to four months prior to admission, she had had gross hematuria four to five days which cleared spontaneously, and one month prior to admission her local physician discovered a mass in the abdomen which he diagnosed as kidney tumor.

The examination revealed a poorly nourished female child. The abdomen was markedly enlarged. There was a large very hard mass in the right upper abdomen extending up beneath the costal margin down below the umbilicus and laterally around the back. It did not move with respiration. The urine was entirely negative on repeated examinations. The hemoglobin was 11.0 grams, 4.310 million red blood count. X-ray of the chest was normal. Intravenous pyelograms showed a normal right kidney. There was no excretion of dye from the left, but a large soft tissue mass was seen in the left upper abdomen. A tentative diagnosis of Wilms' tumor was made and she was placed on preoperative x-ray therapy, which she tolerated moderately well. She returned November 18, 1942, the abdominal mass still being present. On November 20, 1942, a left nephrectomy was performed, the kidney being typical for a Wilms' tumor. Postoperatively, she did well. She returned June 16, 1943, with a metastatic lesion in the right lung and received irradiation for this. She ultimately expired on December 30, 1947. Post mortem examination revealed lobular pneumonia of the left lung but *there was no evidence* of metastatic involvement from the Wilms' tumor.

This is the case of a two-year-old girl who lived five years after a Wilms' tumor was removed and who, at the time of death, showed no evidence of recurrent neoplasm.

Case II. A three-year-old girl was admitted to the University Hospitals on July 23, 1942. She was well until five months previously when she developed nausea and vomiting, loss of strength and pep. The mother noted a lump in the right abdomen two months prior to admission. She had no hematuria and no pain. The examination revealed a firm, smooth mass in the epigastrium extending down half way to the umbilicus and over into the right flank. There was also a discrete hard irregular mass about three by four centimeters just above the umbilicus. The urine was entirely negative. The hemoglobin was less than 7.5 with 2.15 million red blood cells. X-rays of the chest, skull and bones were normal. Intravenous pyelograms showed a mass in the right upper abdomen. The pyelograms were normal, but the kidney was displaced downward by a mass lying above the kidney. A tentative diagnosis of Wilms' tumor was made and she was given x-ray therapy. She returned October 9, 1942. The intravenous pyelograms were repeated. These showed marked regression of the mass in the right abdomen and there was no longer displacement of the right kidney. Chest film was still negative. On October 10, 1942, a right nephrectomy was performed which showed degenerated and hemorrhagic remnants of a retroperitoneal tumor of the embryonal type. She did well postoperatively, but expired January 7, 1943.

This is a case of Wilms' tumor where the present-

ing symptom was gastric disturbance followed by the appearance of an abdominal mass.

Case III. A white female, age 23 months, was admitted to the Pediatric Service on April 23, 1947. The following history was obtained: The patient was in good health until one month prior to admission when the mother, on picking up the child, noticed a firm mass in the left upper abdomen. (This is the typical history given by parents in cases of Wilms' tumor.) She was taken to a physician immediately and he advised no treatment. One week later, the patient developed fever (102 degrees) and the local physician gave her some "fever" pills. The fever lasted three days and then disappeared. The patient was then taken to another physician who referred her to the University Hospitals.

Physical examination was negative except for a large firm smooth mass in the left upper quadrant of the abdomen. The urine was entirely negative. X-ray examinations of the chest were negative, no metastasis being demonstrable. Intravenous pyelograms and retrograde pyelograms established a diagnosis of a Wilms' tumor on the left and a normal kidney on the right. This is described as follows: A film of the urinary tract shows a large soft tissue mass in the left side of the abdomen. Following retrograde injection of the contrast medium, there is a good visualization of the pelvis and calices on the right which appear normal. On the left, there is a distortion of the pelvis and calices with displacement of the ureter toward the midline. A diagnosis of Wilms' tumor was made and the patient was given deep x-ray therapy. A total tumor dose of 2300 R was given. The tumor regressed rapidly and was barely palpable on the last day of the treatment, which was about four weeks after the treatment started. The patient was then permitted to return home to come back to the hospital in six weeks for surgery.

She returned to the hospital on July 7, 1947. At this time, no tumor was palpable and an x-ray of the chest was again negative. Intravenous pyelograms now, on July 7, 1947, following the x-ray therapy, showed the following: The renal pelvis and calices are near normal appearance on both sides and the tumor mass previously seen on the left side has disappeared. A left nephrectomy was then carried out on July 11, 1947. The specimen consisted of a kidney weighing approximately 75 grams which showed in the central cortex, a nodule, roughly round, slightly flattened, measuring four centimeters in diameter. A large portion of the cortex and medulla of the kidney had been replaced by tumor. The outer surface is rough and hemorrhagic. The wall of this portion is lamellated in appearance and in toto is approximately six millimeters thick. The inner portion of the tumor appears to be composed of amorphous necrotic material and blood cells. Multiple sections through the tumor show the capsule to consist of a thick layer of dense hyalinized colagenous tissue which is surrounded by compressed renal parenchyma. Within the capsule are masses of acellular necrotic or hyalinized matrix, in which large clumps of clear foam cells and hemosiderin filled phagocytes are arranged. The center of the tumor consists entirely of acellular necrotic debris. The diagnosis was necrotic tumor of the kidney, presumably Wilms' tumor. No viable tissue could definitely be identified in multiple sections. The patient got along well and has been checked since that time and apparently is thus far doing well. Apparently here we have a case of Wilms' tumor in which the tumor was completely destroyed by deep x-ray therapy.

Case IV. A white female, age 53, entered the hospital on the Gynecological Service on November 1, 1944, complaining of vaginal bleeding. She was in perfect health until two weeks before admission, when she noted vaginal bleeding while taking a bath. She went to her physician who found a vaginal tumor and wished to remove it. Because her daughter was a nurse in this institution, she came to the University Hospitals for further study. There were absolutely no urinary symptoms and her general condition seemed good, although during the past year she had lost some weight. Doctor Randall, the gynecologist, found the vaginal tumor. The lesion appeared to have arisen from beneath the mucosa and extended through it and eroded it. He removed it completely and placed radium about it. This cleared this lesion up completely. The pathological report upon this tissue which he removed was very interesting. It was as follows: "The cells are large and polyhedral with clear cytoplasm. The pattern is suggestive of hypernephroma of genital ridge origin."

Because of these findings, although the original lesion healed, she was referred to the Department of Urology and retrograde pyelograms were made. These were suggestive of either a neoplasm or cyst of the right kidney. There was a very definite deformity of the caliceal system indicating a space-occupying mass in the right kidney substance and a normal kidney on the left side. She was admitted to the Urological Service on January 5, 1945. There had been no symptoms in the interval. The vaginal lesion was completely healed. A nephrectomy was performed on January 8, 1945. This showed a large neoplasm of the lower pole of the kidney which was hypernephroma. Chest film was entirely negative.

This is an interesting case in which the first symptom and sign of a hypernephroma was a vaginal metastasis.

Case V. A white male, age 56, was admitted to the University Hospitals on October 12, 1943. His story was as follows: His general condition had been good. His only symptom had been that beginning about July 1, 1943, he had had several episodes of absolutely symptomless hematuria lasting from one to two days and coming on at regular intervals. There was no pain in the back and no other symptoms or signs. Cystoscopic examination at the time of admission when he was not bleeding, showed a definite papillary carcinoma of the bladder of a low-grade malignancy. It was about an inch and a half in diameter with a rather small base attached to the bladder wall on the right side near the right ureteral orifice. Intravenous pyelograms were made. They showed function in both kidneys and no definite lesion could be seen in them. A diagnosis was made of a carcinoma of the bladder of low-grade malignancy causing the hematuria which the patient had had. On October 23, 1943, a transurethral resection of the carcinoma of the bladder was performed. The pathological diagnosis was transitional cell carcinoma. The patient made a good recovery.

The patient then returned to the University Hospitals on January 12, 1944. He gave the following history: He had gotten along very well until Christmas night, 1943, when he again had gross hematuria. This was seven weeks after his discharge and two and a half weeks before the second admission. Since then, he had noted gross blood in the urine almost every day. There had been no other symptoms. The feeling was, just from the story, that probably a new tumor had shown itself or that there was still tumor present where the previous tumor had been coagulated.

At the time he entered the hospital on January 13, 1944, he was not bleeding. Cystoscopic examination was performed. There was nothing in the bladder from which the bleeding could have come. Therefore, both ureters were catheterized and retrograde pyelograms made. The right kidney was perfectly normal. On the left pyelogram, there was evidence of a filling defect in the pelvis and in the middle and lower calices. A tentative impression was that of papillary tumor of the left kidney pelvis which had produced an implant in the bladder which had first shown itself and had been removed in October, 1943. The patient, the following day, began to have gross hematuria and new cystoscopic and pyelographic examination was made on January 17, 1944. This time the blood could be seen coming from the left ureteral orifice and the pyelogram again showed filling defects in the lower calices. A tentative diagnosis was made of a papillary tumor of the left kidney pelvis and we felt, as I stated above, that the former bladder tumor was a transplant from the renal neoplasm.

Nephrectomy was carried out on January 20, 1944. This showed that we were dealing not with a papillary tumor of the kidney pelvis, but rather a typical hypernephroma involving the lower two-thirds of the kidney and growing on into the pelvis producing the distortions seen on the pyelograms. The patient got along well and left the hospital on the 18th postoperative day. He returned in April of 1944, several months later, with the story that for three weeks he had been having very persistent headaches. Examination showed choked disk and other evidences of brain metastasis. He died on April 29, 1944, of these.

Case VI. A 64-year-old white female entered the hospital complaining of a lump in her right side and weakness of five weeks duration. No urinary symptoms were present. She has been running a low-grade fever during these five weeks; otherwise there have been no signs aside from a palpable right kidney. General physical examination showed a very mild secondary anemia, a white blood count of 8,200, a low-grade fever and a negative urine. The right kidney was easily palpable and quite movable Retrograde pyelograms showed a typical deformity indicating a space-occupying mass involving the right renal parenchyma. Diagnosis was made of a right hypernephroma. On February 3, 1944, eight days after admission, a right nephrectomy was performed with definite improvement in her symptoms. X-ray of the chest had been negative. This is a case where the presenting symptom of a hypernephroma was a low-grade fever and a palpable kidney was the first sign.

Case VII. A white female, age 26, entered the hospital on September 20, 1944. She had been perfectly well until five years prior to her admission when she had gross symptomless hematuria. She visited her physician (remember that at that time she was 21 years of age) who made x-rays and could not find the cause of the bleeding. These were apparently simply a series of plain films of the abdomen. Since then, she had had repeated attacks varying from every two to three weeks to three to four times a year. The bleeding was not severe; the attacks lasted from three to seven days and then stopped spontaneously. No other urinary symptoms had been present. Recently, there had been some pain in the right upper quadrant of the abdomen. No pyuria had been noticed.

General physical examination revealed the following: The blood pressure was 130/70 and the

remainder of the examination was entirely negative. The right kidney could not be definitely palpated. Intravenous pyelograms showed a poorly functioning kidney on the right with a somewhat distorted pelvis. The left kidney was normal. The retrograde pyelogram on the right showed incomplete visualization of the kidney pelvis and calices. The upper pole of the kidneys appeared greatly enlarged with elongation and compression of the upper major calyx and hydronephrosis of the lower portion of the kidney pelvis. X-ray of the chest was negative. The following is an excerpt from a letter written to the home physician: "If the tumor proves to be a hypernephroma (it did), it is the youngest we have had in our series here, since she is only 26 years of age and has a history of intermittent hematuria going back six years. This is extremely interesting. Our youngest case of malignant tumor of this type in the adult, is age 30. It will be very interesting to see what the microscopic study of the tissues shows."

On September 27, 1944, a right nephrectomy was performed. A large solid kidney tumor was present. The pathological report upon this was adenocarcinoma of the kidney. The patient has gotten along splendidly since this.

Case VIII. A 62-year-old white female was first seen in the University Hospitals in May of 1943. She gave a story of having had a good deal of bladder irritability, frequency, burning and smarting, and nocturia over a period of several months. Pyelograms and cystoscopic examination were performed to determine the cause of her difficulties. These showed the following: There was a distortion of the upper pole of the right kidney which was suggestive either of a solitary cyst of the upper pole or a hypernephroma involving the upper pole and distorting the caliceal system. In addition to that, she was found to have a carcinoma of the bladder near the left ureteral orifice. This was thought to be the cause of her bladder irritation. This tumor was resected transurethrally and the base thoroughly coagulated. Her bladder irritation cleared up following this, but she continued to have intermittent gross hematuria. She therefore returned in September of 1943 and at that time, new pyelograms were made which showed the same changes on the right pyelogram. The bladder this time was perfectly normal and therefore could not have been the source of the hematuria. Therefore, in September of 1943, the right kidney was removed. This showed a solitary cyst of the upper pole of the right kidney and not a hypernephroma.

Case IX. A white male, 69 years of age, was admitted to the University Hospitals complaining of the presence of a mass in his right shoulder for the previous four years which had been slowly increasing in size. Examination showed the presence of a poorly nourished white male in no acute distress. On the right shoulder, there was an expansile pulsating mass. On auscultation, a bruit could be heard. There was no evidence of interference with the circulation of the right upper extremity. X-ray examination showed a large osteolytic lesion involving the right clavicle. Intravenous pyelography showed the left urinary tract to be normal; the right urinary tract showed a distortion of the kidney pelvis, typical for hypernephroma.

In this case, there were no symptoms except those of the metastatic tumor. These are extremely vascular and must never be biopsied. A pulsating osteolytic tumor of the bone is, practically speaking, always a metastasis from a hypernephroma.

Case X. A 59-year-old white female entered the hospital on January 28, 1944. She gave the following history. She had been in good health until November of 1943 when she had a fall with trauma to the back. Since that time, she has had occasional severe headache. One week ago, associated with this backache, she had total gross hematuria. This lasted for a few hours and since that time, she has had absolutely no symptoms.

Examination at the time of admission showed her general condition to be good. X-ray of the chest was negative. Intravenous pyelograms showed a normal functioning left kidney with a normal pyelogram on that side. On the right side, although the kidney outline itself seemed normal, there was some distortion of the right kidney pelvis. Apparently the upper pole calyx had become obliterated. This could be due either to tuberculosis or tumor. Cystoscopic examination was therefore carried out. The bladder itself was normal. A catheter was passed up the right ureter to the right kidney pelvis and a retrograde pyelogram made. This showed that the upper calyx filled but was actually a cavity, like an abscess cavity. The preoperative diagnosis was tuberculosis of the right kidney, although no pus was found in that cavity in the upper pole and the bladder itself was negative. Ordinarily, with renal tuberculosis, cystitis occurs and pus is found in an abscess cavity. However, here the kidney outline itself was normal and therefore, neoplasm was not thought of, although a neoplasm of the kidney pelvis could have produced the same effect or a small hypernephroma might not distort the kidney outline on the x-rays and still block off one calyx.

A right nephrectomy was performed on January 31, 1944. Cut section of the kidney showed an epidermoid carcinoma of the kidney pelvis.

The points of interest in this case are that trauma

produced hematuria and this was the first evidence of a lesion of the kidney. The pyelogram was not at all typical for neoplasm. It was rather suggestive of renal tuberculosis. Nephrectomy showed that an epidermoid carcinoma of the kidney pelvis was present.

Case XI. A 53-year-old white male entered the hospital in November of 1943 with an 18-month history of increasing frequency of urination and pain in the left lower quadrant of the abdomen and left flank. This had gradually become worse and there had been progressive tenderness in the left flank associated with chills and fever. There was a progressive loss of weight. Examination showed the patient to be chronically ill with a secondary anemia and evidence of loss of weight. There was a mass that could be palpated in the left flank and this region was very tender. Intravenous pyelograms showed what seemed to be an extrinsic mass impinging on the apex of the bladder but not involving the bladder wall. Cystoscopic examination was performed. The bladder at that time was found to be normal. The right kidney was normal. The left kidney showed what seemed to be a large pyonephrosis. A great deal of pus and peculiar bloody material was removed from the left kidney pelvis. It was thought to be a tuberculous kidney with a great deal of degeneration. Acid fast smears, however, were reported negative. On November 18, 1943, the kidney was removed and was found to be the seat of a very extensive, highly malignant squamous cell epidermoid carcinoma of the kidney pelvis, with a great deal of tissue destruction.

His postoperative course was complicated by a pneumonia from which the patient recovered. He was discharged in good condition.

However, a few months later, he began to have more bladder irritability and cystoscopic examination at another clinic showed the presence of epidermoid carcinoma in the bladder. He was given deep x-ray therapy for this, but in spite of this treatment, he died of carcinomatosis.

This is a case of epidermoid carcinoma of the kidney pelvis, highly malignant, resembling pyelographically, tuberculosis, and giving the history of an infection of the left kidney.

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The Importance of Lymph Node Metastases in Carcinoma of the Cervix Uteri

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Spread of cervical cancer by direct extension is along pathways of least resistance found in laminations of tissue in the paracervical and parametrial regions. Dispersion to regional nodes and to more distant points occurs chiefly through lymphatics, but can be through vascular channels or beneath neural sheaths. It is significant that Mackenrodt's ligament, which is in the normal path of direct extension, contains the main lymphatic vessels of the uterus.

Lymphatics of the uterus form a network with a plexus that converges near the junction of the corpus and the cervix. From that plexus the main lymphatic vessels pass lateralward through Mackenrodt's ligament to form anastomoses with the so-called primary group of nodes situated in the bifurcation of the iliac vessels. A constant set of lymphatics follow the sacrouterine ligament to form anastomoses with sacral nodes forming a portion of the so-called secondary group. Lymph vessels also follow the course of the ovarian veins to connect with secondary nodes higher in the lumbar chain. That pathway may not be too important for cervical cancer, but does present a rather common method of dispersion for endometrial cancer. The lymphatics that follow the round ligaments are of no special significance, but connections between uterine lymphatics and those of the vagina are sufficiently intimate to bring the vaginal tube into one of the more frequent regions of spread. Many of the metastases in that region are trapped in a plexus about the urethra.

It can be assumed that the iliac nodes forming the primary group are the ones most commonly involved, but the numerous intercommunications make impossible any standard method of spread. The incidence of lymph node involvement is probably greater than is generally believed. Most of the data that are available have been taken from the study of tissue removed at operation, and apply, therefore, principally to the primary group. Autopsy studies have been extended to the secondary group and to more distant points.

There is evidence among patients with invasive cancer limited to the cervix itself that about one out of three will show involvement of the primary nodes. Among those with moderate amounts of parametrial invasion consistent with surgical treatment about 50 per cent show positive iliac nodes.

Involvement of the iliac nodes has a serious effect upon prognosis. For a specified stage of clinical advance the survival rate for cases with proven metastases is only half that for those with negative nodes. Adequate treatment of lymph node metastases is, therefore, the critical problem in management of cervical cancer. It is believed by some authors that metastic cervical cancer cannot be controlled by irradiation. The importance of lymph node metastases has been used to emphasize the effectiveness of surgical treatment.

Comparison of surgery and radiation is not easily made. In the attempt to arrive at the relative effectiveness of the two methods one might consider the time factor of reappearance. For both methods of treatment about 60 per cent to 65 per cent of the total recurrence rate will be experienced within the first two years afer primary treatment. From 80 per cent to 90 per cent of recurrences to be experienced will appear within the first five years of observation after treatment.

Neither is there any difference to be found in the location of recurrences. For both methods of treatment about one-fourth of all recurrences will appear in the lower pelvis, including the vagina, rectum, and bladder. Approximately half will be found in the upper pelvis in loose cellular tissue lateral to the uterus. That is the region occupied by the iliac nodes.

In the absence of any distinction to be found upon the basis of time intervening between treatment and recurrence, or upon the location of reappearing tumor, there remains only the possibility of comparing statistics. That is a complex problem, and in a previous paper the attempt was made to compare data published by Bonney with that reported by Waterman. The attempt was made to make the comparison upon a uniform type of clinical material. No superiority was shown for surgery.

Mention should be made of the 224 consecutive patients treated with x-ray and radium in our series now available for five year follow-up. In the entire group the survival rate is 37 per cent. Among those falling into Stage I of the League of Nations classification (i.e. with tumor appearing clinically to be confined to the cervix) the survival rate is 73 per cent. One-third of those patients may be expected to have had metastases to the primary nodes. A survival rate in excess of 66 per cent must be attained, therefore, before there is evidence of con-

trol of any lymph node metastases by irradiation.

Stage II of the League of Nations classification includes patients with parametrial extension to but not attached to the lateral pelvic wall, and with or without vaginal involvement of the upper two-thirds of the vaginal tube. Obviously many of the Stage II patients will be advanced far beyond the commonly accepted operable stage. We can expect an incidence of lymph node metastases in excess of 50 per cent. For the Stage II patients in the consecutive series mentioned above the survival rate is 54 per cent. There is, therefore, indirect evidence that lymph node metastases were controlled in some patients.

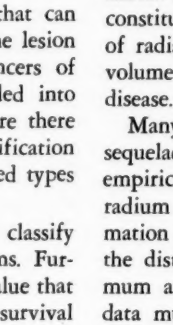
For Stage III the survival rate falls to 14 per cent, and none of the Stage IV patients have survived five years free of tumors. Clinical advance of the disease, often extending well outside the pelvis, is the principal factor responsible for the poorer results obtained in the more advanced stages.

Prognosis depends upon other factors that can be recognized. The gross appearance of the lesion has a relationship to survival rates. Cancers of the cervix can be rather effectively divided into everting and infiltrating forms. To be sure there are cratered lesions that make such a classification difficult. There is evidence that the cratered types are descendants of the everting types.

Among Stage I lesions it is difficult to classify patients accurately into particular gross forms. Furthermore, survival rates are of such a high value that it is difficult to demonstrate difference in survival rates for patients classified into the various gross forms of lesions. Among Stage II patients the difference in prognosis is more evident. For that stage the average five-year value is 54 per cent. Of the 38 patients presenting everting lesions there are 27 alive and well five years after treatment. Among 26 patients with infiltrating lesions only five survived that period. Thus it can be seen that prognosis for everting tumors is much better than the average for that particular stage of involvment, and that prognosis for the infiltrating type is far below the average. It is probable that the poorer result for infiltrating forms is due to a greater tendency toward dispersion.

The normal spread of cervical cancer establishes a "theatre of operations" that defines the volume of tissue to be treated adequately. That volume includes the entire uterus and adnexa, all of Mackenrodt's ligament and the regions occupied by the primary nodes, and the upper third of the vagina. Removal of anything less than that volume of tissue constitutes totally inadequate surgery. Applications of radiation that fail to treat adequately the same volume of tissue cannot be expected to control the disease.

Many radiation failures and most of the untoward sequelae that have followed irradiation are due to empirical methods of treatment. Specification of radium dose in milligram-hours implies no information upon tumor dose. It is important to know the distribution of radiation as well as the maximum and minimum tissue doses obtained. Those data must be correlated with biological effects to be expected in normal as well as abnormal tissue.



Malignant Neoplasms of the Skin

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I think it is well established now that the melanomas originate from the neural crests and actually are epithelial cells; they are neural epithelial cells and, therefore, if they become malignant should actually be called melano-carcinoma, or melanoblastoma rather than melanosarcoma. One of the things that is always confusing when we see these lesions is to determine whether or not they are malignant, whether or not they are dangerous, whether we should fuss with them or whether we should not. I think that one of the things we ought to keep in mind when we deal with the melanomas is first of all that there probably is no person alive who does not have some place on his or her body a cellular hilus which may or may not be pigmented. Therefore, when one considers the incidence of melanoblastoma or melanocarcinoma which is malignant, one must realize that if we all have lesions of that type there are very few of us who develop malignancies from them.

The second thing, I think, is that if we study these lesions from the point of view of a scatter chart (in other words take the front and back of the body and map out on it the location of these lesions in a large number of people), we will find that malignancy has a tendency to occur with the melanoblastoma mainly in limited areas. These areas are the face and neck where perhaps the exposure to sun, irritation from shaving and so forth irritate them, about the genitalia, about the hands, the palms, the feet (and particularly the soles of the feet) and beneath the nails. So there are certain areas where malignancy is prone to develop and there are other areas where it is much less prone to develop. Possibly that is due to the irritation that occurs in these areas.

Another thing which we know about the melanoma is that it has a tendency to have existed for long times, then suddenly it begins to grow. It may be smooth, it may be somewhat shiny, it often is dark colored and it has about it an air and appearance that look as if it was becoming malignant. I still think there is no better criterion as to whether or not a melanoma is malignant than clinical judgment, for I have seen numerous melanomas sent to pathologists when the clinician had every reason to believe that the lesions were benign, and yet, after pathological study, they were reported to be malignant. I have talked with numerous pathologists about their criteria for the diagnosis of malignancy and each will admit that it is just his opinion. They actually cannot be sure. In those cases where the lymphatics and the blood vessels are packed with melanoma cells, that is a different matter. But in many of the melanomas that we see it is very difficult for the pathologist to say "that is a malignancy" or "this is not a malignancy."

No melanoma should be treated with x-ray because these cells are not sensitive to x-ray. In fact x-ray may seem to be a stimulus rather than a cure in this disease.

Some of these lesions show a tendency for the pigment to begin to float out from the melanoma itself. Whether there is any direct relationship between the pigment and the malignancy is one of the things we don't know, and yet those of us who have watched these melanomas will often find that as the malignancy occurs the pigment does have a tendency to float out of the melanoma itself. There is an old axiom that if a nevus is hairy it has a tendency to be much less malignant than one which is devoid of hair. That is an axiom which is not always true, for I have seen malignancies in hairy nevi. Nevertheless, many of the ones that we see that we find later to have been malignant are smooth, shiny and often darkly pigmented lesions.

Perhaps some of you have seen in Indians or the Chinese, particularly in childhood, a bluish lesion on the back extending over the pelvis itself, usually over the hips and sometimes extending onto the back. That is known as the mongolian spot. It actually is a group of pigmented nevus cells but not of the epidermal type. Those nevus cells are actually of the connective tissue type. That lesion may exist in some of us aberrantly as the blue nevus which is a sarcomatous lesion, and not a carcinomatous lesion.

The epidermal nevus shows throughout the epidermis islands of pigment and you find the cuboidal nevus cells. These have a tendency to end just about at the end of the epidermis, and for this reason this is sometimes called the junction type of nevus, in other words limiting itself to the epidermis. Again this is the type that is a melanocarcinoma if it becomes malignant.

The blue nevus is almost always a benign lesion. Should it become malignant, however, it becomes truly a melanosarcoma and not a melanoblastoma or melanocarcinoma as does the ordinary pigmented nevus. This, then, is an entirely different type which is probably a vestigial remnant in certain people of the old mongolian spot and therefore has a different origin, a different prognosis and less tendency to become malignant than does the ordinary cellular

or blue nevus or the cellular pigmented nevus that we so commonly see.

I should like to continue with some of the epidermal neoplasms and take up one that is frequently overlooked or thought to be a patch of seborrheic or neurodermatitis. It is seldom thought to be carcinoma. Many times it will occur on various parts of the body; it is erythematous, it has sometimes a little bit of scale, it often has existed for many years in the same area and if you ask the patient who has it he will tell you perhaps that it has been slowly growing. It may be made up of tiny little nodules or it may have a fine thread-like border around its surface. Sometimes as it grows it has a tendency to heal in the center and then be active around the border itself. This epithelioma can be a basal cell epithelioma, which remains in the epidermis itself and therefore becomes an intra-epithelial epithelioma. At times it may be a lesion which is called Bowen's disease, a sharply circumscribed lesion which pathologically shows a tremendous amount of dyskeratosis of the cells and looks like an extremely malignant lesion. The only lesion that is similar pathologically is Paget's disease, and many times it is difficult to differentiate this lesion from Paget's disease. I have seen one example of it where this type of lesion actually was around the area of the nipple extending to the nipple itself and down the ducts. A pathological section through the nipple showed typical Paget's disease and a pathological section through the adjacent skin showed the so-called Bowen's disease—in other words, the two diseases were in the same area and type of skin. This is also a carcinoma but it has the characteristics in practically all instances of the basal cell carcinoma—a tendency to grow by extension and not to metastasize. It can, however, assume fairly large proportions.

Another example of this lesion shows a fairly large irregular lesion of many years standing with a tendency to heal in the center and proliferate around its edges. One of the things that we have often learned about neoplasms is that once a cell is malignant it has a tendency to remain malignant, and yet that is not true in all the instances of the intra-epithelial epithelioma. I have seen some of these lesions where the border itself was entirely active and where the center was entirely scar. A biopsy of the border will show a basal cell carcinoma, the center will show nothing but fibrous tissue covered with perfectly normal epithelium; yet from the story of the case the center at one time was also a malignant lesion. It seems possible, in some of these lesions at least, that as they progress and grow around their border they have a tendency to heal and scar in the center and the epithelium that eventually covers that scarred area is normal epithelium.

These lesions can be excised, they could be cauterized and curetted, or they can be treated with x-ray. They are perfectly benign lesions in that they have a tendency just to extend in the skin itself. They do not metastasize, and yet at times they can be multiple and many of them can be present in the same individual.

Now I should like to consider another lesion of the skin which is common and that is the lesion that begins in a place of leukoplakia. I think one of the things which we should remember about lesions of the lip, as we should about lesions on the back of the hands, is that if they begin to degenerate and become carcinomatous they are squamous cell carcinomas. One of the things that one notices here is also a thing that is common. We have patients who have leukoplakia on the lower lip but without any leukoplakia on the upper lip. The typical case is a man whose skin is fair, whose hair is red, who has had considerable exposure to the sun, the sun striking the lower lip predominantly and starting the leukoplakic process there. There is no question in the minds of most of us now that in so far as the skin is concerned, the sun is one of the carcinogenic agents as found in nature.

In a recent article by Dr. Fletcher Hall of Santa Monica, he tried to correlate the color of the hair, the color of the eyes, and the character of the skin with the incidence of carcinoma, and his figures showed that the best correlation between carcinoma and one of these three is actually with the color of the eyes. The greatest correlation occurred (about 85 per cent) in the person with blue eyes. Therefore a blue-eyed individual is more prone to develop carcinoma of the skin from light than is the brown-eyed individual, regardless of the color of the hair or regardless of the character of the skin.

Leukoplakia can, of course, occur from other agents too. We know that irritation of any kind, whether it be light, snuff, tobacco, pipe-smoking, cigarette smoking and so on, is certainly one of the causes. That, however, does not explain why women will develop leukoplakia and eventually kraurosis of the vulva, because there is an area which is not exposed ordinarily to irritating elements, and yet leukoplakia does occur and kraurosis does occur and the incidence of carcinoma in those lesions is relatively high. Dr. Miller was interested in that problem not long ago and in several of his cases, after he did a plastic repair of the vulva itself, found that in the areas of skin replacing these that had been removed, it wasn't long until these new areas of skin became leukoplakic too. It was of interest that, during the study which he was making, I also ex-

amined the mouths of those women, and found that there was no correlation whatsoever between leukoplakia of the vulva and leukoplakia of the other mucous membrane. We do not know exactly what it is that causes these lesions in women.

If we have leukoplakia on the lips, we ought to make sure that there is not leukoplakia of the mouth. One individual, I think, demonstrates a cause of leukoplakia on the hard palate. There was thickening of the skin and discoloration of the teeth by tobacco. He was a man who smoked a pipe, the smoke of which would come up against the hard palate, and he developed a rather extensive leukoplakia on the hard palate.

Other individuals again give away their story—one can see the discoloration of the teeth stained with tobacco. One can see the beginning of a definite leukoplakia on the buccal mucous membranes in the mouth. There is no question that some people are more prone to develop leukoplakia than others. It seems to be an intrinsic character and therefore, if irritation comes in regardless of the cause of the irritation, leukoplakia is apt to result.

What should be your attitude in the management of leukoplakia? Should you attempt to destroy it when you diagnose it or should you tell the patient you will have to watch it and have him come in every six months in order to examine the leukoplakic areas and determine whether or not they should be destroyed or whether he can go on for another period of six months? I have taken the latter view in that leukoplakia is precancerous. It is a lesion which may break down some day and show a carcinoma— and often a squamous cell carcinoma. Hence, any area of leukoplakia, regardless of the age of the person, should, if there is any doubt, be biopsied and studied pathologically to determine whether or not the area has already become malignant. If one can be fairly sure that the area has not changed, that there are no thickened areas greater than the surrounding tissue, that there are no nodules in the area, I think one can safely say, "You can let that go for another six months but should any change occur in it, you let me see it." I have followed some fairly extensive cases of leukoplakia for many years without seeing any degenerative changes in those areas. On the other hand, if there is a little area of ulceration, or if there is a little tendency for tumefaction, it should be immediately biopsied, and if found to be malignant of course the entire area should be destroyed or treated with roentgen therapy.

We have a patient who is a fairly young man who presents several things that one can see objectively. In the first place his tongue looks a little larger than the normal tongue. In the second place he has disturbing leukoplakic areas on the tongue itself. The third thing that one can see is a definite nodule, and there are also rough and jagged teeth which are a source of trauma, with a resulting ulcerated lesion and a perforated area which looks like an ulceration below that patch of leukoplakia. This man has a gumma of the tongue, and gummatous tongues are made up of nodules in the tongues themselves.

Many times in a gummatous tongue (which is an asymptomatic tongue as far as the patient is concerned) leukoplakia will follow, and after leukoplakia carcinoma. One of the things that always crosses my mind when I see rather extensive leukoplakia of the tongue is this. Does this patient have a gummatous tongue, and how do I know that? First of all, gummatous infiltration of the tongue causes the tongue to be somewhat larger than normal; secondly, one should always palpate those tongues because if they are palpated one will not only be able to feel larger nodules than in this case one could see, but one will also feel nodules all through that tongue. Thirdly, one ought to take a serological test, and fourthly, one ought to keep in mind that a long standing gummatous tongue is a precancerous tongue.

For a period of time, we did neck gland resections routinely in all malignant lesions of the lip. I don't think that was a particularly good idea because the incidence of involvement of the neck glands was only between five and 10 per cent. We did away with clinical judgment entirely. Since that time we have been a little more conservative; we have allowed the physician to be a physician and prognosticate whether or not he thought metastases had occurred after an examination of the lesion, determination of the grade of malignancy of the lesion, and palpation of the neck glands. By so doing, using selected cases, we have now increased our ability to prognosticate the presence or absence of neck gland metastases in a fairly good percentage of our cases—better than 75 per cent. We do not do routine neck gland dissections now in those cases where we have reason to believe that the lesion is relatively early, where there is no regional adenitis, and from our clinical judgment the lesion is early enough so that metastases are relatively unlikely.

On the other hand, when one gets a patient with a fairly large carcinoma of perhaps two or three years duration, one may and often does, find definite metastases in the neck itself. Of course in those cases the neck gland resection should be done along with treatment of the primary lesion whether it is by surgical excision or roentgen therapy.

A squamous cell carcinoma which begins in a senile keratosis has large amounts of hyper-keratosis, but at the base of it you will find a squamous cell

carcinoma of relatively low malignancy. These lesions are frequently of many years duration, and sometimes if they are allowed to grow untreated they form enough keratosis that they become cutaneous forms. They almost always are much less malignant than the ulcerative lesions that one sees in the neck or the lip, but nevertheless they are squamous cell carcinomas. In many instances, however, as there are no metastases, these lesions can be treated locally and the results are much better than they are in the more rapidly growing lesions. These cutaneous forms can occur in any location.

Carcinoma of the tongue, as you all know, is one of the worst lesions that we have to treat. Some occur without any evidences of a leukoplakia. Metastases may occur in the neck glands or they may be back in the planes of the tongue, and hence one cannot be sure whether dissection of the glands in the neck, with the hemi-destruction of the tongue surgically or by x-ray therapy, is adequate treatment. Time is the only method that we have to tell whether our treatment has been successful.

It is usually a rule to assume that those lesions which occur on the face above the line of the mouth itself are basal cell carcinoma. An example of such a carcinoma is sharply circumscribed, has a definite pearly border and sometimes a dome surface or sometimes an ulcerative surface. It is a lesion which grows by extension, and consequently a lesion which, if handled properly, will give excellent results. One of the things that we forget so often, however, in dealing with the basal cell carcinoma is that the lesion, though it looks sharply circumscribed, may have little projections of epithelial cells going out into the subcutaneous areas which may start new islands of basal cell carcinoma around the borders. That is why it is wise in the treatment of these lesions to make sure that one goes out well around the border of the lesion itself, whether it be for a surgical excision or cautery destruction or for x-ray therapy. Dr. Moe of the University of Wisconsin, as you know, has had the opportunity to follow some of these by using fixation in situ. He can pick out these little ramifications of the basal cell epithelial prolongations and has been able to follow them out quite a distance from the original focus—with this information he has destroyed the entire lesion.

Clinically you cannot always be sure that these are basal cell lesions because there is a medial cellular carcinoma which occurs frequently above the lip, and probably it is not a true combination of basal and squamous cell. It probably is a tumor like the basal cell carcinoma which arises from the appendages of the skin such as the pilus sebaceous apparatus. Its prognosis is not the prognosis of squamous cell carcinoma, as it does not metastasize to distant areas through the lymphatics or blood stream, but has a tendency to grow by extension like the basal cell carcinoma. Therefore, it should be managed just like the basal cell carcinoma.

One of the problems that we have in managing basal cell carcinoma is that of lesions near the eye itself, perhaps extending to the mucous membrane of the eye or even down on it. One is confronted with a therapeutic problem here. If we treat this surgically may we not produce an ectropia, or destroy the papillae so that tearing will occur from the corners of the eye? If we treat it with x-ray are we going to destroy the papillae itself and the duct that leads into the nose to drain off the tears? I believe there is adequate evidence now to state that if we treat these patients by x-ray, exposing adequately beyond the margins of the lesion itself but covering the eyeball with a silver sheet, and if there is not already carcinomatous infiltration into the duct itself, we will not destroy the duct. Therefore, in lesions of this type it is my humble opinion that the best treatment we have is x-ray and not surgical excision.

Another lesion of course that we are confronted by is the lesion that may be along the ala of the nose. This is a fairly deep lesion. If we are going to destroy it what is going to happen to the cartilage? Is the cartilage going to be affected, and if the cartilage is affected is that going to have any permanent effect on the nose? This lesion too can be destroyed by x-ray and I have not had, in my experience at least, any changes that I thought were important in the cartilage of the ala from roentgen therapy. This lesion can also be treated surgically, but to me x-ray in such an area is the best form of treatment.

We recently saw a man who was red haired, an Irishman who lived in the northern part of the state. He lived in the woods and had multiple carcinomas all over his face—senile keratoses, a basal cell carcinoma, and a squamous cell carcinoma with metastases in his neck. In other words, he had almost all the types that one finds on the skin. He had done nothing about them and said he was old enough that he didn't think they would ever kill him, yet he had metastatic lesions when he was treated at the hospital. He is a man who illustrates the fact that after the skin begins to degenerate, it may degenerate into both basal and squamous cell lesions. And he is an individual too who had many methods of treatment. The senile keratoses were excised surgically, other lesions excised or treated with x-ray, and a neck gland resection was done on one side. Many times it is necessary to use several forms of treatment in order to give the patient his best chance.

When we see a basal cell carcinoma which has

been neglected or poorly treated to begin with, and has extended to adjacent areas or even into the external auditory canal—even deeply enough so that it involves periosteum or the outer table of the bone—we have a therapeutic problem of some importance. In such a case the best thing that one can do is to treat the entire area with x-ray.

Lesions on the hand are squamous cell carcinoma in practically every instance. They are commonly in red haired, fair-skinned individuals, associated with senile keratoses. These are lesions which should not be neglected. They have a tendency to remain in situ for a long period of time before metastases occur, but metastases can and frequently do occur and therefore one of the things that one should always do is to examine the epitrochlear gland and the axillary glands in people who have lesions of this type.

Again the hands of individuals who have had too much roentgen exposure may show telangiectasia, atrophy of the skin, multiple senile keratoses, and squamous cell carcinoma. There are also changes in the nails that are characteristic of roentgen changes. These are not always physicians; occasionally they are individuals who have had too much x-ray treatment by a physician for dermatitis of the hands over a long period of time and developed these roentgen changes that eventually led to carcinomatous degeneration.

If the carcinoma of the hand is poorly treated or neglected it can produce an extensive squamous cell carcinoma that may require an amputation of the hand itself, with extensive resection of the glands in the axilla and epitrochlear region, with still a chance that none of it is enough.

Another of the things that is definitely carcinogenic is arsenic. In the area where I live where there are orchards, arsenate of lead is one of the forms in which patients get arsenic. Again Fowler's solution and the Asiatic pill are still used considerably in the treatment of disease, and there are several proprietary medicines on the market which contain arsenic. Things for which we ought to search when we see an individual who has a carcinomatous degeneration of his skin which we suspect might be due to arsenic, is the typical rain drop pigmentation which is often associated with it and the punctate keratoses on the palms and soles.

To differentiate from these we have carcinomatous degeneration in the scar of some previous disease such as lupus vulgaris that has healed. It may be a long standing, chronic, destroyed, lupus erythematosus which has resulted in carcinomatous degeneration; it may be in the scarring that occurs following an actinomycosis which has been destroyed in early youth, and which has left a scar. It may be carcinomatous degeneration in an individual who has had roentgen therapy—even 15 or 20 years previously for such ill advised reasons as epilation.

Cancer of the Breast

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It is with great pleasure that I am here to discuss a subject of prime importance to all of us, physicians, surgeons, graduate students, undergraduate students, and the laity. Carcinoma of the breast is the most common malignant disease in the female sex, and second comes carcinoma of the cervix. We have had a most excellent presentation this afternoon on what should be done for the latter.

If doctors would only consider every patient who comes to them with a lump or a bump in the breast to have a cancer, we would make many earlier diagnoses. If we would prove either that it is or is not a cancer of the breast many more would be saved.

The American Cancer Society is making a strong effort to discuss the problem with the laity and make them cancer conscious. In the majority of instances this is a good thing, as only a few people get cancer phobia. The Society is also extremely interested in the education of the undergraduate student, the graduate students, and the residents in the hospitals. They are especially interested in discussing these problems with our confreres, the doctors who are in practice, the doctors who see these patients first. The cancer detection clinics that are being organized all over the country, I believe, will eventually be discontinued, as soon as they have fulfilled one of their main purposes, namely, to draw to the attention of the doctor in his office and in the clinic the fact that he must ever be cancer conscious. Every doctor can be a cancer detection clinic by himself if he will be cancer conscious, and actually perform a thorough and complete physical examination himself. The importance of this thought I can impress upon you with two experiences I have had in the past few weeks.

Two fine women in their early 50s came under my care with advanced, almost hopeless carcinoma of the breast, and both had been under the care of physicians. They had not neglected themselves. They had gone to their doctors and in one instance the doctor followed his patient for three and a half years with a lump in her breast. She was going through her menopause and the doctor told her all women at the time of the menopause had lumpy breasts. "Go home and forget about it." She would return to him and ask him, "Are you sure, doctor, that this is not a cancer?" He would say, "Oh, don't worry about it, it's not a cancer."

The other lady developed a thrombosis of a vein just under the skin in the upper outer portion of her breast. She went to a doctor five months ago, and the doctor, realizing that it was a thrombosed vein and feeling a swelling in the axilla behind the border of the pectoralis major, said that it was an inflammatory mass. The thrombosis of the vein he thought was the result of inflammation. He put her on penicillin for a long period of time. She asked him, "Are you sure it isn't cancer?" He said, "Of course not. The vein will re-canalize, the swelling will slowly disappear and you are going to be all right."

Two days before New Year she was going to leave for Florida. She was worried about the swelling and wanted to see the doctor again. He was away on a short holiday, and she went to his associate. He immediately was suspicious that the lump under her arm might be a cancer, and he sent her to a surgeon. The surgeon saw this patient and he also was suspicious of a carcinoma. When finally I had to operate upon her, about 10 days ago, it was practically a hopeless case. All of the nodes in the axilla were involved with carcinoma right up to the very apex and the primary tumor in the breast was only as big as the nail of my little finger. She had large, fat, pendulous breasts, and it was only with the greatest difficulty that we could find the primary tumor on palpation. The metastatic node mass in the axilla had been the cause of the thrombosis of the vein.

Both of these women had been under the care of doctors. We doctors assume a tremendous responsibility if we tell a patient with a lump in the breast to go home and not worry about it, to forget about it.

Naturally, not every lump and bump in the breast is a cancer, and we must consider the various possibilities of differential diagnosis. I do not want to take too much time to go into the various points of differential diagnosis in detail, but I do want to mention a few of them and to draw to your attention the importance of what we should advise the patient to do.

First of all, the inflammatory conditions in the breast. There we have acute and subacute inflammation, tuberculosis, specific disease, syphilis, the mycoses, and such conditions as Boeck's sarcoid or plasma cell mastitis. Then we have the congenital abnormalities of the breast, where we have asymmetry of the breasts, which we can find out by a careful history. We may have the hypertrophy of the breast and a very important point, the supernumerary nipples and breast gland tissue which can

occur anywhere along the nipple line. Above all we have the accessory mammary gland tissue that occurs in the axilla behind the pectoralis major muscle, in which carcinoma not so rarely develops. When it does develop in this accessory mammary gland tissue in the axilla, it is usually serious and more malignant than the carcinomas in the breasts themselves.

We then have the functional disorders. Anyone who works in a breast clinic knows that the majority of patients who come, come because they complain of pain in the breast and it is the pain in the breast that usually does not denote malignancy. It is called mastodynia, or pain in the breast, and upon careful examination, lumpiness usually just before the menstrual period is found. It disappears after the menstrual period, and all we have to do is to reassure the patient, have her put on some hot compresses and tell her to wear a well fitting brassiere.

We also have the benign tumors that occur between the skin and the breast. Those are the lipomas, the fibromas, and the hemangiomas. Surgical excision is naturally indicated.

We then come to the other benign tumors that occur in the breast. I will rapidly go over them: fibroadenomas, single, discrete, like marbles. You can roll them under your fingers. Always advise excision. They occur in young women. Never leave them there, but if you excise them, gentlemen, especially if you should do it in your office, never throw the lump in the pail. Every specimen that you ever remove from any part of the body must be examined pathologically. We then come to adenofibrosis, or fibroadenosis, which some doctors call adenosis of the breast. Formerly we called it Shimmelbusch's disease. It presents disseminated swellings in the breast, often with a sharp margin at the breast margin, which you can usually lift away from the chest wall as if you lifted a saucer away from the chest wall. The patients always complain of pain and tenderness, and you immediately become suspicious and know that it is probably not a carcinoma. This is a condition that can improve with pregnancy and lactation, just the opposite of carcinoma, which is made worse by pregnancy and lactation. Here occasionally local excision of the area, if troublesome, is indicated. Once in a while simple mastectomy becomes necessary. This condition usually occurs in the small atrophic, non-fatty breast.

Then we have the giant mammary myxoma. It is the condition that Johannes Müller described years ago as cystosarcoma phyllodes and occurs with sudden rapid growth of a tumor which has been present in the breast for a long time. A fibroadenoma that has been present for many years and then suddenly begins to grow into a big bulky mass should make one suspicious of cystosarcoma phyllodes of Johannes Müller, the giant mammary myxoma. Simple mastectomy with careful histological examination will relieve this condition.

Then we come to the simple cysts. The simple cysts are caused by blockage of the ducts. If they are filled with dark fluid, they are called blue domed cysts of Bloodgood. Aspiration of a cyst, as taught by some doctors, is a perfectly legitimate method of treatment. The cyst will collapse and in many instances will not recur. But, I warn you of two facts. If you aspirate a cyst of the breast and find bloody fluid, think of the fact that you may have a carcinoma in the wall of that cyst, or if you aspirate the cyst and it collapses and you examine immediately afterwards and still find an induration in the breast in the region of the simple cyst, you may have a carcinoma. Therefore, personally, I always excise a cyst so that I can obtain a histological examination and can carefully examine the breast in the region of the cyst at the time of the operation.

Now a few words about what we used to call chronic cystic mastitis. A better term is cystic disease of the breast. Cystic disease of the breast is often bilateral. It usually occurs in the upper outer quadrants of the breast and the ducts are filled with debris and with hyperplastic epithelium. As the disease goes on, patients complain of pain in the breast. The cysts that develop may be from two to three millimeters in size up to three to five centimeters in size. As you examine those patients, make a careful notation on your chart of the location and size of the infiltration. Never tell the patient to go home and forget about it, but always tell her, "I do not believe that you have carcinoma. There are none of the clinical signs of carcinoma, but you have an abnormality in the breast and I must re-examine the breast every three weeks at the beginning, later every six weeks, and then follow it every two or three months."

If the area of induration of cystic disease persists, I always advise segmental resection of that breast, like cutting out a piece of pie, suturing the breast together and obtaining a most careful pathological examination. If the pathologist reports that there is marked hyperplasia in the lining of the ducts or in the lining of the cysts, we may then have a precancerous condition. As Warren of Boston has shown, there is a higher percentage of later development of carcinoma in the breasts that contain cystic disease if we have marked hyperplasia.

With intra-ductal papillomas, the patient comes complaining of a little serous or bloody discharge on the brassiere or nightgown. With careful examination you usually find a small swelling directly under the nipple and the areola. You may be able

to feel the swelling, namely the papilloma, inside of the dilated duct. It is the one condition where transillumination of the breast is of real value. With a good transilluminator, like the Cameron breast transilluminator, you may be able to see the dilated duct with blood in it. It will help you to know where to make the incision in order to dissect out that duct with the papilloma. This procedure will cure the patient. If there is bloody discharge and you cannot find the duct with the papilloma but by gentle pressure on the different segments of the breast you see where the bloody discharge comes out of the nipple, then occasionally you are forced to remove that sector of the breast, and follow with a most careful pathological examination. Or, if you have a persistent bloody discharge from the nipple without palpable tumor and you cannot find the segment or quadrant of the breast from which the discharge comes, and especially if it is dark bloody discharge and the woman is in the cancer age, you must strongly suspect the presence of a duct carcinoma. A simple mastectomy is indicated with almost serial section examination of the breast by the pathologist Frequently a carcinoma is found and you will then immediately go ahead with the radical operation.

Finally, a few words about traumatic fat necrosis and plasma cell mastitis. They are included in the differential diagnosis. Traumatic fat necrosis usually occurs in a large fatty breast with a history of injury and ecchymosis and a following tumor in the breast. With that history, no retracted nipple, no adhesion of the skin, and no axillary lymph nodes, think of traumatic fat necrosis. Simple excision with pathological diagnosis will cure the patient.

The condition of plasma cell mastitis has been described by Adair, Cutler, Ewing and other authors. Here you have the history of an inflammatory condition of the breast with local redness but not during lactation. When redness and inflammation subside, a tumor in the breast remains at that site with all the clinical signs of cancer, a retracted nipple, adhesion of the skin, edema of the overlying skin, and axillary lymph nodes. However, you have the history of previous inflammation and redness in a non-lactating breast. Then think of plasma cell mastitis and do a local excision with a careful pathological diagnosis to be sure you are not dealing with carcinoma.

Finally we come to Paget's carcinoma of the breast. If there is ulceration of the nipple of long duration, especially if it is in a young person, it may be a dermatological problem. Always do a Wassermann. But if the history is of short duration, and there is ulceration of the nipple, think of Paget's carcinoma which develops in the ducts directly underneath the nipple. The malignant Paget's cells grow outward along the ducts onto the surface, and with disturbance in nutrition and circulation of the nipple, ulceration occurs and one has all the signs of Paget's disease or Paget's cancer of the breast. This is a malignant condition which metastasizes early to the regional lymph nodes and requires radical mastectomy.

This then brings us to our main subject, namely "Cancer of the Breast." At the present moment, gentlemen, more lives are saved by radical mastectomy than by any other method of treatment. Let us remember that! Early diagnosis is vitally important, and let us also remember that 50 per cent of all cancers of the breast occur in the upper outer quadrant, in the same area where cystic disease is so prevalent. To make the diagnosis of cancer of the breast is a vitally important subject, just as important as the operation itself. The technique of the examination is as important as the technique of the operation, because with both procedures we can seal our patient's fate, especially if improperly executed.

Unfortunately pain is not an early symptom. The patient usually discovers the painless lump in the breast by accident. We can frequently make the diagnosis of cancer of the breast upon inspection alone, and that is a vitally important point. We can at least become so suspicious of cancer of the breast by inspection alone that we hardly have to palpate the breast in order to confirm the suspicion. And why is that so important? Because, the gentleness of examination is so important. Frequently in cancer of the breast, tumor cells are present in the lymphatics. There may also be tumor cells within the blood vessels, because the tumor cells grow through the wall of a vein into the lumen of the vein. They never grow into the lumen of an artery. If the tumor cells are in the vein, and if by rough examination you break off two or three of those tumor cells from the tumor thrombus in the vein, then those cells become tumor emboli and float into the blood stream. No matter how you then treat that carcinoma locally, either by x-ray or good surgery, the patient's fate is sealed, because there are already distant microscopic metastases, which at present we have no method of diagnosing or detecting. The physician, by his examination of the breast, may possibly have brought that about.

Similarly, with the present teaching that women should periodically examine their own breasts in order to discover lumps, we must always add that if the woman examines her own breast she MUST examine it gently, because one can readily see that a woman, by her own examination, being worried and afraid, can break off tumor cells and spread them into the lymphatics and into the blood stream.

By inspection of a patient you observe the level of the nipples, which way the nipple points, whether

you see a swelling in the breast. If the patient puts her arm up over her head in good light, you may see the swelling, you may sometimes see the little dimpling of the skin, and you immediately become suspicious of the presence of a carcinoma. If you have the patient bend forward and let the breasts hand away pendulous from the chest wall in good light, you may also sometimes see the swelling, you may see the dimpling of the skin and again may make a tentative diagnosis of cancer of the breast. Then you observe whether there is any edema, which is called peau d'orange, of the skin.

Following inspection comes palpation, and this again must be most gentle and light. The patient first lies down with the arm up over the head, putting the pectoralis major muscle on the stretch, inclining the body a little bit to the opposite side so that the breast flattens out against the chest wall and you can then divide the breast into four quadrants. Take a little bit of talcum powder and sprinkle it on the skin of the breast, and starting at 12 o'clock with the lighest touch you draw your hand over the breast from the periphery towards the nipple. Then with the same maneuver you examine the various radiants, at one o'clock, two o'clock, three o'clock, etc. You will find that your fingers will glide over the skin easily on account of the talcum powder. You will feel how your fingers come up over a little swelling just as you go over the crest of a mountain in an automobile. So you can make the diagnosis by the *gentlest* of examination.

Then you examine the nipples. You first draw one forward lightly and then the other one forward lightly and by comparing the two you can tell whether one is being held down a little bit more than the other. If you find that one nipple is being held down, you know that you are probably dealing with carcinoma. If by taking the overlying skin very gently and rolling it with your fingers over the swelling that you have discovered, and find you cannot roll the skin, or if there is any puckering of the skin, you will know that the skin is being held down by the septa that go from the skin down to the breast gland and the tumor. This will give you further confirmation of a suspicion of a carcinoma.

Naturally always examine both breasts. Then carefully examine both supraclavicular fossae for lymph nodes. After that the patient may sit up. By gently laying the breast on one hand, you may gently palpate with the other hand to confirm the findings with the patient lying down. Never take the breast in your hand and squeeze it and thereby pump tumor cells into the lymph vessels or into the blood vessels.

The examination of the axillae should also be gentle. Remember that we are correct in only about 30 per cent of our preoperative examinations of the axilla. That has been shown in various papers that have been written. If the axilla contains much fat, unless there is a fairly large, and therefore late, advanced metastatic lymph node, you may miss the tiny little nodes, which, however, may be solidly replaced by carcinoma. You cannot feel those small nodes with your fingers. The examination of the axilla is performed by *gentle* palpation with the flat hand and fingers against the chest wall with a forward and backward, and upward and downward stroke.

Naturally a complete physical examination is most important. Never fail to do a rectal and vaginal examination. We have seen patients with a lump in the region of the breast which proved to be a secondary metastatic deposit from a carcinoma of the cervix. If one performed a radical mastectomy on such a patient without having done a vaginal examination and a speculum examination, how embarrassed one would be to later receive a report of metastatic cervical carcinoma.

X-ray examination, if available, should always be done. The chest should be x-rayed. If the tumor is in the inner quadrants of the breast, also do a lateral x-ray view of the chest. In these cases there may be enlargement by metastasis of lymph nodes in the anterior mediastinum. We have been able to make a diagnosis of a metastasis to an anterior mediastinal lymph node of the internal mammary series of nodes on the lateral x-ray view. Scout films of the skull, the spine, the pelvis, and the long bones should be done if possible and available. Always remember though that a negative x-ray report does not mean that microscopic metastases are not present. It just shows that there is no far advanced metastatic carcinoma.

Now a word about biopsies. There are various methods of doing a biopsy. At Memorial Hospital in New York they have developed a technique which in their hands seems an excellent method of doing a biopsy. This is the aspiration biopsy. In their hands and with their pathologists and with their team work, it apparently works out well. A small nick is made in the skin and an 18-gauge needle with obturator is introduced into the tumor. With a well fitting 20 cc. Record syringe, aspirations are made in one, two, or three directions. The aspirated material is expressed onto a glass slide and a smear made. This is stained and examined.

Personally, we think that we would rather teach the profession as a whole all over the country to excise the entire tumor, if small, using a cautery knife, if you have one available, to go through the skin and through the breast, sealing the lymphatics, and taking the fascia over the pectoralis major muscle along.

If a pathologist is available have him in the operating room, and then let him cut across the tumor, and, usually nine times out of ten, you can make the diagnosis on gross pathology, which is then confirmed by frozen section examination.

If a pathologist is not available, then send the specimen to the nearest pathologist as quickly as possible, tell him that you want a report in 24 or 36 hours, and if it is a carcinoma he should telephone or telegraph to you, so that the radical operation may be performed as quickly as possible after the diagnosis has been made. If the tumor is large and bulky a section may be cut out of the tumor, the wound then swabbed with pure carbolic acid, and the skin sutured. The biopsy incision is always sealed.

What must the surgeon know if he is going to operate for cancer of the breast? He has to know the lymphatic drainage area of the breast and where the cancer cells can spread. They spread either by way of the lymphatics or by way of the blood stream. The surgeon must know the principles of the radical operation. These principles were laid down 56 years ago, independently, by Halsted in Baltimore and Willy Meyer in New York. This was in 1894, and those principles of the radical operation are as true today in 1950 as they were in 1894.

And what are they? Wide excision of the skin, thin skin flaps, the removal in continuity of the breast containing the tumor, with the regional lymphatic field, which means the pectoralis major and minor muscles, the meticulous dissection of the axilla by *sharp* dissection, with fine surgical forceps and a very sharp scalpel, removing the sheath of the axillary vein, dissecting the subscapular space way up behind the axillary vessels, preserving, if possible, the long thoracic nerve of Bell and the thoracodorsal nerve, but sacrificing them if involved in tumor tissue, taking the fascia over the latissimus dorsi, the subscapular and serratus anterior muscles and the intercostal muscles, dividing the fibers of origin of the pectoralis minor, then going to the opposite side of the sternum and removing the fascia from the opposite pectoralis major where the perforating vessels go through to the mediastinum, dissecting from the opposite side across the sternum and ending by dividing the fibers of origin of the pectoralis major and dividing the perforating vessels on the side of the lesion. Personally, we take the anterior sheath of the upper portion of both recti muscles. The wound is then flushed with saline and closed. If the flaps cannot be brought together, a Thiersch skin graft is immediately placed on the defect and a proper kind of dressing applied. Those are the principles of the radical operation.

Now another vital chapter. What are the principles of good cancer surgery technique? Let us remember that any surgical procedure must be performed with good technique, but it is not as vital for the future of the patient and the life of the patient as the technique required when we operate for cancer. When we operate for cancer there is great danger of cancer cell implantation in the extensive wide open wound. If cancer cell implantation occurs in a radical mastectomy we will experience early local reappearance of carcinoma in the field of operation. If one employs careful cancer surgery technique one can prevent this to a large degree. In our own cases we experience less than six per cent of local reappearance in the field of operation. Our patients who die following radical mastectomy die more frequently from distant metastases, not of local reappearance. What are these principles?

Number one, cover the clock in the operating room. It does not make any difference how long the operation takes as long as you do a meticulous operation, have good anesthesia, blood transfusion available, and do not leave a good deal of dead tissue in ligatures. Cushman Haagensen at the Presbyterian Hospital in New York makes a very apt remark, which I like to repeat, because it brings a message. He does not mean it literally, but it brings a message to the profession who operate for cancer of the breast, and he says, "An operation a day keeps the cancer away." Now what he means is, no matter how long the operation takes, we have a job to do and we have to do that thoroughly and carefully.

Secondly, never put a sharp retractor on the tumor side and then on the tissue side. You may implant cancer cells. Frequently change the scalpel. Cancer cells have been recovered from the edge of a scalpel. Frequently wash your hands in the wash basin and have the basins changed, because Dr. William Crawford White of Roosevelt Hospital in New York has proven by centrifuging the solution water in the basins that cancer cells are present in the wash water in which you wish your gloves. Never use a hemostat a second time without washing it and reboiling it, because on the end of the hemostat, where you clamp a blood vessel, there may be cancer cells.

Keep the field covered. Expose only the small field you are operating on, and cover the remainder with large laparotomy pads. Finally, do not have tens of hemostats on the tissues, because the assistant, by moving those hemostats back and forth, with the weight of those hemostats may press tumor cells into the lymphatics and into the blood vessels. Stop frequently and ligate, getting rid of the hemostats. Use the cautery on the tumor side, and cotton or silk on the tissue side for hemostasis. This

saves time. These are the principles of good cancer surgery technique and they are as important as the diagnosis and any method of treatment.

I must also say a word about the criteria of operability. This varies greatly with different surgeons and clinics. There is unfortunately no common denominator of criteria of operability and therefore it is difficult to try to interpret the statistics as published.

We try to operate upon every case in which we think that we can adequately remove the cancer field in continuity. We include those cases that have skin ulceration and those that have axillary metastases, even nodes that are fairly large, and in certain of these cases the axillary vein also has to be resected.

There are certain contraindications to the radical operation. These are:

1. The inflammatory type of carcinoma with redness of the skin, marked peau d'orange and edema of the skin of the breast and the arm. Harrington of the Mayo Clinic, however, has recently reported some surprisingly good results with radical mastectomy in this type of case.

2. Metastatic skin nodules at a distance from the tumor—the so-called cancer en cuirasse.

3. Extensive supraclavicular lymph node metastasis or involvement of the opposite axillary nodes.

4. Carcinoma of the breast during pregnancy or lactation, although Adair and Harrington have recently reported remarkably better results in some of these cases operated by the radical operation.

5. Evidence of distant metastases, especially skeletal or visceral, unless a local palliative procedure is decided upon.

Now let us turn to some lantern slides. This slide shows accessory mammary gland tissue which may occur from the axilla through the nipple down on the abdomen to the pubis to the inner side of the thigh where you may have accessory mammary gland tissues.

In these slides you will see the lymphatics studies of Oelsner, Most, Sappey, and Proirer and Cuneo. These we must know. The breast drains toward the midline down towards the abdomen, then out toward the axilla where the lymphatics run between the pectoralis major and minor muscles to the lymph nodes that lie along the subscapular space, and then into the axilla from the latissimus dorsi as the outer landmark to the very apex of the axilla. These lymph nodes lie and are attached to the sheath of the axillary vein. A lymph vessel runs along the cephalic vein to a lymph node which lies between the deltoid muscle and the pectoralis major. On cross section you can see, and this is a very important point, that in tumors of the inner half of the breast the cancer cells may pass with the perforating vessels and enter the lymph nodes that lie in the anterior mediastinum along the internal mammary vessels. From there they can go along the intercostal muscles to the posterior chest and to the nodes that lie along the vertebral column and then in front of the vetebral column from where they can go to the lungs. From the outer portion of the breast the lymph vessels go into the axilla.

Sappey has shown many years ago, recently confirmed by the son of Sampson Handley in England, that important lymph nodes lie in the anterior mediastinum especially in the second, third and fourth intercostal spaces along the internal mammary vessels. Handley has shown that these nodes are frequently involved in metastases. Recently he has been making an incision in the second intercostal space, early in the operation, especially in tumors in the inner half of the breast, and has exposed these lymph nodes and taken them out. If metastases were found by frozen section he has not continued with the radical operation. Sappey has also shown that lymph vessels go along the intercostal muscles and enter the lymph nodes that lie along the vertebral column and from those lymph nodes cancer cells can directly enter the thoracic duct and pass up the thoracic duct and enter the circulation. You may readily see how easily and quickly metastases in this part of the body can develop.

Geschickter has written one of the best books on breast diseases. I will show you one of his excellent charts, which shows how important it is in the radical operation to remove the pectoralis major and minor muscles because Rotter's node lies right in between the two muscles with many lymph vessels. Here are the lymph nodes along the internal mammary vessels and here the lymph vessels that go down to the falciform ligament, showing the importance of removing the anterior sheath of the recti muscles. Here are the lymph nodes in the subscapular space and along the axillary vein. We must also know anatomy. No surgeon should operate for a carcinoma of the breast without reviewing the anatomy, especially if he performs this operation only occasionally. He must know immediately exactly where he is, and what each structure is, which one he can sacrifice and which he should try to preserve.

This is another valuable chart from Geschickter's book. Anybody who sees a lot of breast disease, who will study this chart, will quickly realize its worth. It shows the solitary tumors, the soft tumors, the multiple diffuse tumors, the firm tumors, those that occur in the periphery of the breast and those

in the central portion of the breast. The black little circles over the nipple denote bloody discharge from the nipples, the clear circles denote serous discharge. A careful sutdy of this chart will teach innumerable, valuable points in diagnosis of breast diseases.

These slides show carcinoma metastases in a lymph node, carcinoma cells as a tumor thrombus inside of a vein, a carcinoma metastasis in the alveolus of a lung, the embolic spread I have spoken about.

The late Jonathan Wainwright of Scranton, Pennsylvania, in the 1920's, proved in these sections of the entire breast how important it is to perform the operation in a radical manner. In this section you see the nipple, the carcinoma, the dilated ducts and stasis; here you see below the nipple two simple cysts and right next to them a carcinoma. This points out the importance of the fact of multiple tumors in one breast that I told you about. Here is a simple cyst and the lining of this simple cyst is solid carcinoma, which one can sometimes suspect if there is bloody fluid in the cyst or if induration persists after aspiration. This shows the spread of cancer of the breast along the septa that pass between the fat cells, the cancer cells passing along them into the overlying skin. This fact shows the importance in the radical operation of removing all of the skin of the breast, and when you have made the incision to dissect back very thin skin flaps, in order to prevent early reappearance of the carcinoma along the scar line or close to the scar line.

In this slide are cancer cells in the lymph vessels between the pectoralis major and minor muscles. This proves the vital importance of removing *both* pectoralis major and minor muscles in continuity with the breast. In this section of Wainwright, in the fat of the axilla, you can see these tiny little lymph nodes completely replaced by carcinoma which one cannot feel on palpation.

These slides are Halsted's original pictures of 1894. They show the tumor, the wide excision of the skin, the incision out on the arm and the dissection from the sternum outward. He originally left the pectoralis minor muscle in place and divided it, retracted the upper end, performed the axillary dissection, and then re-sutured the pectoralis minor muscle. He removed the pectoralis major.

Dr. Willy Meyer, on the other hand, in the incision that you see here, immediately advised at that time—1894—(these were his original pictures drawn from a cadaver) division of the pectoralis major muscle at the humerus, the pectoralis minor at the coracoid process, the dissection of the axilla, dissecting across the chest wall from without medially and dividing the fibres of origin of the pectoralis minor on the chest wall and the pectoralis major at the sternum.

These following slides show the technique we now use which is the Willy Meyer technique with some improvements. You see the incision up on the arm, here the fixed point between the clavicle and the axilla and down on the abdomen.

Then in the next picture you see the incision at the very margin of the breast with the tumor being in the center, and here you see the incisions joined and the very thin skin flap, showing how thin the skin flap is made, leaving all the fat behind on the tissue side, and you see the land mark of the latissimus dorsi. A little path is cut along the latissimus and at the base of the flap across the chest wall to the midline, and here you see a similar path cut from the suprasternal notch along the opposite pectoralis major down to and across the recti muscles, after reflection of the medial flap.

All the hemostats are frequently removed, lap pads cover the wound not being worked on. Then you start with the axillary dissection. Here is the pectoralis major, the cephalic vein, the tendon of the pectoralis minor showing through, and you see the pectoralis major insertion divided, exposing the coracobrachialis, and here is the pectoralis minor tendon divided at the coracoid process. This then exposes the axilla.

The pectoralis major is divided along the clavicle and the axilla is dissected from within outward by meticulous sharp dissection. You see here the axillary vein completely freed of its sheath, here are the large lymph nodes. One black silk marking thread is placed at the very apex of the axillary dissection for the pathologist and two black silk marking threads at the outermost portion. The pathologist will then know that all of the axillary nodes must lie between the two markings. It depends a great deal whether nodes are involved in the outer portion of the axilla or at the apex of the axilla, as to the prognosis in the individual case. Here you see the subscapular space dissected out, the long thoracic nerve of Bell and the thoracodorsal nerve.

And now the dissection goes across the chest wall ending near the sternum. A lap pad is placed on the chest and the breast is allowed to drop back. The dissection continues from the opposite pectoralis major, taking the sheath of the recti muscles and finally dividing the fibres of origin of the pectoralis major on the tumor side. This is the wound at the end of the operation showing the deltoid muscle, the cephalic vein, coracobrachialis, axillary vein, long thoracic nerve of Bell, thoracodorsal nerve, the latissimus dorsi, serratus muscle, ribs with the intercostal muscles, the upper end of both recti muscles

all dissected free and clean of fascia, and the opposite pectoralis major. Then you flush the wound with saline. The wound is sutured with multiple interrupted sutures, if necessary suturing the skin edges to the intercostal muscles, if the wound cannot be closed primarily, and immediately putting on a Thiersch graft, taken from the thigh.

The Thiersch graft is dressed separately. One of the most important points is to express all of the air and blood, especially from under the clavicle and axilla. I believe a great deal of the complication of edema of the arm comes from collection of serum which you have to repeatedly aspirate. Low grade infection may cause some of the edema of the arm which is so annoying. Then you put the dressing on, carefully making compression in the axilla with cotton waste or fluff gauze. You next see the specimen as it goes to the laboratory, all of the skin of the breast, the anterior sheath of both recti muscles, the opposite pectoralis major fascia, the subscapular area, and here the axilla with the one black silk thread at the apex and the two black silk threads at the outermost portion of the axilla, and here you see the specimen dissected showing a tiny little primary tumor in the breast, with the very large metastatic lymph nodes in the axilla. Here is the patient after the operation with the Thiersch graft healed and with full motion of the arm.

This is another patient, a most interesting case. This photograph was taken nine years after a radical mastectomy with axillary lymph node involvement. I did a gall bladder operation on her when I returned from the service and she seemed perfectly well. Two years after the gall bladder operation, nine years after the radical mastectomy, she developed a mass in the right lower quadrant, and we explored it. We took out a lymph node. The lesion was inoperable. The lymph node showed a metastasis from her original breast carcinoma. Those tumor cells must have been lying there asleep in that pelvis. We don't know what the inhibiting factor is, nor do we know what the inciting factor is, that will make those tumor cells that lie asleep, dormant for many years, finally come to life and grow like wildfire.

Here is a case of bilateral carcinoma of the breasts. This is a patient whom we operated on, and three weeks apart did a bilateral radical mastectomy. We lost track of her on follow-up after five years. Last year she walked into my office and here is her picture 25 years after the bilateral mastectomy. Therefore bilateral carcinoma should not be a contraindication for radical operation.

Male carcinoma of the breast is usually very malignant. Here is a man with carcinoma of the breast. He had all of the axillary lymph nodes involved and in this instance we did a supraclavicular lymph node dissection. We have not had a single patient who has had supraclavicular lymph node involvement who survived five years. This man lived for four years and nine months and on my return from the service he had no local reappearance of carcinoma but he had pleural metastases from which he died.

Here we see another man with carcinoma of the breast. He had a radical mastectomy, just the same as in the female, and here you see him after the operation. Here you see another man ten years after radical mastectomy with a large Thiersch graft on his anterior chest wall.

Now a word about local reappearance and palliative surgery. You see here a patient three years after a radical operation which I personally did. In the center of the Thiersch graft there is a local reappearance on the chest wall. In these cases we cut a window out of the chest wall if there is no evidence of distant metastases. Here is the specimen with the reappearance cauterized, the section of the chest wall with the three ribs removed, with the pleura underneath. It is very quickly and easily done under endotracheal anesthesia, and then you take a pedicle skin flap from the abdomen below, swing it up, sew it into the defect, blow up the lung, and the lung will immediately become adherent to the fat on the undersurface of the flap. This patient lived for three years after the operation, and then died of liver metastases.

Dr. George H. Semken, my former chief, showed a patient at the New York Surgical Society who lived for 10 years after such an operation.

Here is a patient operated on elsewhere with an incomplete operation and preservation of the pectoralis major, local reappearance here and the surgeon then excised it locally and swung a little pedicle flap into the defect. Shortly thereafter, another local reappearance occurred. In such a situation, you can either do a very wide excision or use irradiation. I chose to do a wide excision as you see by this specimen here. Here is the original small flap in the specimen. The new pedicle flap is not taken from the region of the operation but a large pedicle flap is taken from the abdomen with the pedicle behind. It is swung up in place and the donor area is decreased in size and a dermatone graft used to close the remaining defect. This patient has gone for a year and a half without local reappearance.

Here is a patient who had x-ray therapy for carcinoma of the breast. She was the mother of a doctor. She refused operation and was treated intensively by x-ray. She developed x-ray dermatitis.

But she still had carcinoma and she had infection, fever, and terrific pain. She was with her son down in Texas, and he telephoned me and said, "Doctor, you have to do something for my mother even if she dies on the operating table." She came up, and I found the tumor fixed to the chest wall. I excised the breast tumor, chiseled away some of the sternum and again took a large pedicle flap from the abdomen, swinging it up into the defect. She also had metastases in her axilla.

I had to divide the operation into two stages on account of the infection. Six weeks later I excised the axilla. I took the skin of the axilla to which the tumor was adherent, together with all of the axillary contents, the muscles and the axillary vein, removing the whole vein. You can see in this incised specimen how the carcinoma was adherent to the skin of the axilla. Then I took a pedicle flap from the back, lifted it up, swung it into the axilla, to take the place of the skin that had been removed, and you see here that the flap fills in the axilla. The interesting thing is that while I had told the family that the patient would live for only a few months, she has now gone for a year and a half with no clinical evidence of the disease. That is palliative surgery. We do not do it with the idea of arresting or curing the disease. She will surely die of carcinoma, but she has gone for a year and a half in complete comfort, no pain, no more fever, no more morphine.

This patient came to us with a frozen axilla after an incomplete operation, a simple mastectomy. She had terrific pain and morphine would not relieve her. Our neurosurgeons tried to see what they could do with neurosurgical procedures. They could not relieve her and the patient pleaded that something be done for her pain. Here we did an interscapulo-thoracic amputation. In the specimen you see the ulceration in the axilla and the whole shoulder girdle removed. A flap was swung up covering the chest defect with a graft. All of the brachial nerves were invaded by cancer. She lived for two years in solid comfort, without morphine, and then died of general carcinomatosis.

I show you these slides just to impress you with the fact that palliative surgery may be of inestimable value for the patient in some of these cases. It does not improve one's own statistics. However, that fact does not influence me.

Now finally one word about the use of hormones in the treatment of advanced and inoperable carcinoma. Remember, gentlemen, that we are only at the threshold of our knowledge, it is all still experimental, we change our ideas all the time. Here you see an advanced case with nodules in the skin, in the supraclavicular fossa and up in the neck. She also had skull metastases which you can see here in the skull. She was put on androgens, 100 mgm. of testosterone propionate three times a week over a long period of time. After about three months almost all of the nodules had regressed, the mass in the supraclavicular fossa regressed and she went along for almost a year with a regression of her carcinoma. No hormone treatment has ever arrested the disease but it does cause regression. It often relieves pain and the patients no longer require morphine. It is of definite value in some cases.

Now here is a patient who was also put on androgens for bony metastases following a radical operation. I personally did not perform the mastectomy. She was sent to me for a chest wall resection, but on account of the distant metastases she was put on androgens, she has gone for two years, and she is still alive in comparative comfort.

Here you see a patient in our breast clinic who refused all form of treatment, either irradiation or surgery. She was put on estrogens because the carcinoma was of soft parts, and she was past the menopause. She received diethyl-stilbesterol, 15 mgm. a day in three divided doses, and she took that for two years. This photograph was taken at the beginning, and after two years her condition was exactly the same as when we started. It did not advance and it did not regress.

Here you see a case of bilateral Paget's cancer. It is very extensive with cancer en cuirasse. Palliative x-ray treatment was of real help, together with hormone therapy.

In this slide you see what may occasionally happen with postoperative irradiation. We do not use irradiation postoperatively with the surgical technique as we do it. However, if the surgeon does not take much of the skin of the breast, or if he does not make very thin skin flaps and if he does not do a meticulous sharp dissection of the axilla, then there is no question but that postoperative irradiation is indicated. However, if you make very thin skin flaps, and even if the postoperative irradiation is given expertly, this slide shows what may happen. An extensive hole has been burned right through the skin flap in the axilla.

Finally the last slide shows the picture of an incomplete operation. The pectoralis major and minor muscles have been left in place, a simple mastectomy with a half baked axillary dissection has been done, and the patient comes to our clinic with an early reappearance, three months after the operation. These cases make us most unhappy and dissatisfied with some of the surgery that is performed for cancer of the breast. Therefore, in closing I would like to

make this remark. Does one feel satisfied when one sees a patient like that?

I always like to quote the late Dr. John B. Deaver of Philadelphia. He used to say to his assistant at the end of an operation, "Gentlemen, what are we now?" The assistant was trained and he said, "Satisfied, Dr. Deaver." Dr. Deaver would turn to his audience and he would hold up his hand and say, "Gentlemen, gentlemen, what it means to be satisfied." I always believe that if we are going to use surgery in the treatment of cancer, then we should feel satisfied at the end of the operation that we have done all that could possibly be done surgically for the patient.

The Cutaneous Manifestations of Lymphoblastomata

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I realize that in anyone's practice the incidence of lymphoblastoma is relatively uncommon. I do feel that many times cases come into our office that we may miss unless we are conscious of the cutaneous manifestations.

One type of lymphoblastoma that is often misdiagnosed is confused with an exfoliative dermatitis from drugs such as arsenic, or an exfoliative psoriasis, (because psoriasis can be generalized and can produce a picture simulating this). Another thing that can be confused with this type of lymphoblastoma is a sensitivity to such things as ragweed which might have caused a generalized dermatitis. Those are all possibilities, and for that reason I think a good name to call a disease of this type when one first sees it is an exfoliative erythroderma—in other words an exfoliative dermatitis characterized by redness of the skin. I think that one should also keep in mind, when one sees an exfoliative dermatitis of this type, that this might be the onset of a lymphoblastoma.

Now supposing that this is a lymphoblastoma. In the first place what would one do to prove it, and if it is a lymphoblastoma is it one which has special characteristics? Can one say from examination of such a patient that this lymphoblastoma is the beginning of Hodgkin's disease or is it a leukemia or is it a type of lymphoblastoma that the dermatologist calls mycosis fungoides? There is no way to tell at this stage. Any one of the lymphoblastomas, even a lymphosarcoma, can begin as an exfoliative erythroderma.

One of the things that I think is always worth doing when one sees a patient of this type is first to find out how long this exfoliative erythroderma has lasted. How did it begin? Did it begin as a nondescript dermatitis or did it begin perhaps as a rather sudden burst of a generalized dermatitis? Secondly, does the patient have an adenitis? After all, any patient who has this generalized exfoliative erythroderma as we see it here will have an adenitis regardless of the cause of that erythroderma, because with the loss of the epidermis in sheets, as it often is lost in these cases, secondary bacterial agents come in and there is apt to be a dermatitis. Therefore, feeling an enlargement of the inguinal glands, the epitrochlear glands, the axillary glands, the cervical glands and so on does not mean that one is dealing with a lymphoblastoma. One should always keep in mind that in the lymphoblastomas there is an adenitis and that is one thing that is helpful. One should also determine whether or not there is enlargement of the liver and of the spleen, and of course do adequate blood studies on these patients.

Now biopsy of the skin is very often helpful, particularly in the lymphosarcomas and the leukemias, but many times in the other forms of cutaneous lymphoblastoma the skin biopsies, unless they are read by one well trained in the diagnosis of skin pathology, may not be helpful. Therefore, in these cases I think it is advisable not only to get a skin biopsy but also to get a biopsy of the gland, for sometimes although the skin may not be pathologically pathognomonic the gland may be. In addition to the biopsy of the skin and the biopsy of the gland one should also do adequate blood studies on these patients.

This exfoliative erythroderma may be generalized. The thickness of the skin is evident by the rather coarse folds over the knee. That skin pathologically shows considerable edema, and one can also see the swelling of the ankles and the swelling over the dorsum of the feet that is again part of the edematous process of the disease. Again keep in mind that patients can and sometimes do have the onset of their lymphoblastoma in this manner.

Now we will consider a dermatological disease that had been believed for many years to be an entity. It has been called by an unfortunate name and that is mycosis fungoides. It is characterized by the appearance in the skin of a nondescript dermatitis which at times looks much like a contact dermatitis. It may look like a seborrheic dermatitis. It may be an exfoliative erythroderma as we saw a moment ago. Or there is another manifestation which is called the tumor type, characterized by a sudden outburst of one or more tumors appearing in the skin. This lesion is characterized by an opaque reddish colored tumor which has definite infiltration. It is entirely asymptomatic in this stage, because usually these lesions do not itch, whereas in the nondescript dermatoses itching does occur and in the exfoliative erythroderma there usually is considerable pruritus. But often in the tumor stage as one sees it here the lesions are not pruritic. There are no excoriations that one can see, and if one biopsies that lesion one gets a pathological picture most dermatologists think is characteristic of the disease—mycosis fungoides.

If this disease is allowed to progress without diagnosis, or without treatment, or if a person who has it thinks it is probably a form of eczema and

doesn't do anything about it, he may develop a scaling plaque of erythroderma whereas the skin nearby is normal. One can see that this is more than the ordinary eczema-like dermatitis. This is something that is infiltrating the skin; there is a definite border around it; there is considerable scale. If one feels it, it has a definite sense of depth and it actually is an infiltrative disease of the skin. In some areas one sees a definite tumor. This tumor may have existed long enough that the center is ulcerative. These tumors are often likened to a rotten tomato because they have a tendency to appear, the center apparently has the vascularity destroyed, and ulceration occurs producing a manifestation of this type of lymphoblastoma that is called mycosis fungoides—a fungating disease.

We saw a patient not too long ago who was sent in to have an amputation of the arm because of the sudden onset of a tumor which had a sort of moulage appearance—in other words a certain unreality in its appearance due to the fact that there was a tremendous infiltration of cells into one area giving a light color, again the beginning ulceration in the center of the tumor and again a lesion which pathologically and from its clinical course fits in this entity that we call mycosis fungoides.

Another man that we had not too long ago had a single tumor appear on the knee, which was large, rapidly growing and with ulceration in the center—a highly malignant lesion. Pathologically it gives a picture like mycosis fungoides or granuloma fungoides.

A woman is now in the University Hospital who had her first tumors of this type—large, fungating masses of necrotic material and granulation tissue which produced bleeding. There had not been any pruritus around these, but many of the other lesions which she had on her face, trunk and extremities were extremely pruritic. Some of these are coming up as tumors. Many of them have been excoriated. There are some scratch marks which are deep enough to have taken out the entire surface of the epithelium. She has had these lesions about the mouth.

Another woman appeared to have a factitial dermatitis, except for a multitude of tumors that were in big fungating masses on the scalp. At the time that she was seen, of course one of the things that was thought was whether or not this was a factitial dermatitis and whether or not these weren't secondarily infected, pyogenic lesions on the scalp. A biopsy of the lesions, however, showed the characteristic infiltrations of a lymphoblastoma.

The so-called mycosis fungoides being superficial, as it is in most instances, is just as amenable to roentgen therapy or other types of therapy such as nitrogen mustard, urethane, and pyrobenzamine acid as are the other lymphoblastomas. Because the lesions are cutaneous they can be diagnosed early in their course, and it is because the roentgen therapy can be given adequately to the surface lesions that the response is actually more dramatic than it is in Hodgkin's disease.

Now if we take a pathological section of a patient who has this so-called mycosis fungoides we find a tremendous infiltrate. It is often described as a band like infiltrate extending deep into the foramen, and if we look at it under high power we find polymorphonuclear cells, eosinophiles, lymphocytes and occasional plasma cells. We find cells undergoing mitotic phases. This polymorphous infiltrate is believed to be one of the characteristics of this lesion and at times we find cells in which there are more than one nucleus—in other words cells that are something like the Dorothy Reed cell but not quite like it. It is because of this somewhat different pathological picture in the skin—a somewhat different multinuclear giant cell that one sees—and also the fact that mycosis fungoides has a tendency to be a cutaneous disease, that most of the histopathologists of the skin have believed that mycosis fungoides was a lymphoblastoma of a different type than Hodgkin's and lymphosarcomas.

On the other hand in a recent study that we are now completing we have had the opportunity to perform autopsies on 10 cases of mycosis fungoides which were typical in so far as the cutaneous manifestations were concerned and we have been able to show in every one of these 10 cases that the disease has not been cutaneous alone, but it has involved many of the structures of the body, even the heart itself, and that in every single instance where we have had the opportunity to study it pathologically that these patients either have a lymphosarcoma or that they have Hodgkin's disease. In other words then the cutaneous picture is a different picture but if you have the opportunity to examine infiltration of the other visceral portions of the body, the lymph glands, the spleen, the liver and its other viscera one finds that this disease falls into the class of either Hodgkin's or lymphosarcoma and that makes one think again that perhaps mycosis fungoides is a clinical diagnosis like erythema multiforme and yet pathologically it is probably either Hodgkin's disease or lymphosarcoma.

Now the other lymphoblastomas may have their onset again with an exfoliative erythroderma or they may present themselves as diseases with characteristic infiltrations in the skin.

The first lesions that a young woman had noticed were plum-colored lesions. That color is due to the infiltration in the skin of masses of white blood cells. In this particular case the woman had a myelogenous leukemia. We know, however, from

other cases we have seen and from reports in the literature that the lymphocyte has a tendency to produce a purplish color in the skin if it invades the skin in large enough numbers. But on the other hand so does the monocyte myeloblast. And, therefore, if one sees a person who has tumors sharply circumscribed, non-pruritic, and plum-colored one can say that in all probability this is either a lymphatic leukemia or a myelogenous leukemia. These lesions are not hard, often they will show some gangrenous necrotic areas in them, and there may be some scale. But again once one has seen lesions of this type one can almost always make a diagnosis of one of the two types of leukemia that produce them.

The third lymphoblastoma which produces by far the most cutaneous manifestations is one of the less common types of leukemia—the monocytic leukemia. About 50 per cent of the cases of monocytic leukemia will have cutaneous manifestations. A young woman came into the hospital because of hypertrophic gingivitis. This was the thing that bothered her. She did have one solitary lesion in the chin but that was the only cutaneous manifestation. The gums look semi-transparent due to the fact that there is a tremendous infiltration of cells in them; they are friable and have a tendency to bleed just from the mastication of food. There are few diseases that will produce a hypertrophic gingivitis like that. We are all acquainted with the fact that scurvy does, and if you have ever read any of the old accounts of scurvy among the sailors of the old sail-boating days you get the idea that scurvy could produce a marked hypertrophic gingivitis associated with bleeding of the gums not unlike this. But scurvy is a very rare disease today.

Another disease that produces hypertrophic gingivitis which you have all seen, I am sure, is dilantsia. Individuals who have taken dilantin for long periods of time because of epilepsy may develop a rather striking hypertrophic gingivitis, not only of the gums, but sometimes of the hard and soft palate. And again we see hypertrophic gingivitis in individuals who traumatize their gums a lot like the man who chews a cheap brand of scrap tobacco and gets a lot of dirt in it, or children who because of one reason or another (usually because of psychiatric difficulties), get in the habit of chewing gritty things and driving this material into the gums themselves and producing hypertrophy of the gums. This is not an uncommon finding in monocytic leukemia, and if any of you have, in the next year or so, a case of monocytic leukemia one of the things that one ought always to look for is the hyperplastic gingivitis that so frequently is a part of this disease and may be one of the first manifestations of it.

The lesions of monocytic leukemia are often a little different than they are in lymphatic and myelogenous leukemia and they are also different than they are in Hodgkin's disease and lymphosarcoma. You can see two types of lesions: one of them is tiny little violaceous rather discrete papular lesions which are much lighter in color than are the lesions of myelogenous and lymphatic leukemia; the other thing is the purpura that is associated with the decrease in the platelets.

One patient, who is a physician, had two lesions —one on his thumb, and one on the palm of the hand. He came into the hospital because of these lesions. As they came up he thought perhaps they were due to some foreign body, but they didn't disappear. Both were excised, and we found that when a pathological section was made they also were nodules of moncytic leukemic infiltration of the skin. This man died about three months later of his monocytic leukemia. Therefore, of the various lymphoblastomas one should keep in mind that of the leukemias the one that most commonly causes cutaneous infiltration is monocytic leukemia.

True Hodkin's disease of the skin is very very uncommon, and I think perhaps it is uncommon because the things that we call mycosis fungoides are in all probability Hodgkin's disease. To find the picture of true Hodgkin's disease of the skin so that one can look at the skin and compare the pathological changes there with the pathological changes that one finds in the lymph glands is a rare thing. Many times when we see Hodgkin's disease of the skin and can make a diagnosis of it pathologically we find first of all that it is usually associated with a great deal of pigmentation. It secondly is associated with a terrific pruritus so that many times these patients, before they have any lesions whatsoever, will come to a physician because of extreme itching. He will go through the various and sundry causes of itching, find nothing that has relieved this patient, and eventually think of the possibility that perhaps this is a lymphoblastoma. And by doing biopsy studies of the skin and the glands they will eventually arrive at a proper diagnosis.

I can recall not so long ago a woman who was in the hospital for a long period of time because of an extreme pruritus. One of the things that we had in mind when we first saw her was that she might have a lymphoblastoma. We could find no evidence of it whatsoever, but in one lateral view of her mediastinum we did find what we thought perhaps was a slight amount of widening. We asked our own x-ray department in the University Hospital to give her roentgen therapy to the mediastinum and because of the lack of evidence and because of the fact that there wasn't enough enlargement of the

mediastinum to warrant it they refused to do it. We sent her to another hospital where the roentgenologist did x-ray her mediastinum and within a week's time her pruritus disappeared and was gone for a year. She eventually got a recurrence of the adenitis of the mediastinum and in the abdominal region, and at this time the adenitis was diagnostic by x-ray and the glands in the abdomen were palpable. She again got x-ray treatment and she again lost her pruritus. But one of the things that one ought to keep in mind in any of these patients where you can rule out the common causes of itching is that you may be dealing with a lymphoblastoma and this lymphoblastoma may be a Hodgkin's disease.

Lastly I should like to mention one thing that has been of considerable interest to us. A woman who was a patient in the Blood Institute of our university was treated for myelogenous leukemia. She had been under treatment for about a year and a half. On her next examination at the hospital she had an irregular ulcerated crusted lesion of the face and lips and she also had a lesion on the forehead which looked much like a rather large acne pustule. We were asked to see her at that time, and one of the routine things that we do is a culture for the mycoses. She grew from these lesions a pure culture of torula histolytica. These lesions that she had on her forehead and these tiny lesions which she had on her face were characteristic acne-form lesions of a disseminated torula histolytica infection.

In going over the literature I was interested in one of the reports of the Massachusetts General Hospital conferences where Dr. Mallory said, in a discussion of a torula histolytica case, that much to his surprise, as far as he could remember practically every case of torula histolytica he had seen was in a case of lymphoblastoma. We went back over our own series of cases, of which we have had five in the past five years, and three of our five cases have had lymphoblastoma.

We have also been interested in the association of lymphoblastoma and histoplasmosis. In the examination of the 88 case reports in the literature of histoplasmosis, five have had some form of lymphoblastoma. Now that is interesting from this point of view. Does the lymphoblastoma have anything to do with the invasion of the body by one of the deep mycoses or do the deep mycoses have anything to do with the production of the lymphoblastomas? Those are questions that I cannot answer, but I do believe that the lymphoblastoma itself in all probability prepares the soil for the invasion of the deep mycosis.

One woman did not have the meningitis that is so often the characteristic of torula histolytica. She had nothing but lesions of the skin insofar as we could tell at the time, but we watched her spinal fluid, which eventually became positive for the torula histolytica organism, and she eventually died of a torula meningitis. It is interesting that two of the deep mycoses—histoplasmosis and torula histolytica—would have a tendency to invade lymphoblastomatous tissue.

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The Surgical Treatment of Carcinoma of the Stomach*

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A review of over 14,000 gastric resections for cancer of the stomach by Pack and Livingston[1] in 1940 revealed that if every patient with gastric carcinoma entered the best surgical clinic in the world, 95 per cent would remain uncured and approximately 90 per cent would be dead of their disease within 18 months.

In reviewing the various factors responsible for this low survival rate the following considerations have been stressed:

(1) In 50 per cent of the patients the disease is so far advanced that the condition is considered inoperable without exploration.

(2) Another 25 per cent of the cases are found to be inoperable at exploration.

(3) There is 10 to 15 per cent immediate mortality rate following resection.

(4) Of those patients surviving resection, two-thirds are dead in three years; three-fourths are dead in five years and four-fifths are dead in 10 years.

(5) Thus, two to six patients are left out of the original 100 who survive 10 years or longer.

The greatest loss occurs in those patients who are considered inoperable when first seen and a vigorous campaign has been and still is being waged to educate the public to seek attention early and to keep the members of the medical profession alert to the recognition of the symptoms of gastric cancer.

Several new methods which may assist the physician in detecting early asymptomatic malignant gastric lesions are at present being investigated in various hospitals. None, however, has been developed sufficiently to be adapted to general usage on a large scale.

The routine use of gastric analyses as a screening devise with further investigation of cases found to have achlorhydria of gastric secretions has been investigated by Niazi, State, Trelor and Wangensteen.[2]

Adapting the technique of exfoliative cytological diagnosis to the detection of gastric cancer by studying the gastric secretions or gastric washings for the presence of malignant cells has been reported by Graham, Ulfelder and Green,[3] and others.

Roach, Sloan and Morgan[4] are studying the practicability of the routine photofluorographic examinations of the stomach in certain groups of patients. In an analysis of the first 6,000 patients so examined 36 were found to have the accepted radiological manifestations of carcinoma, and the diagnosis of malignancy has been confirmed at operation in 23 of these patients. This series included both symptom free patients and patients who came to the hospital with gastro-intestinal complaints.

A simple accurate systemic test for the presence of a malignant lesion in the body would be of great aid in detecting asymptomatic gastric neoplasms as well as many other types of early malignant lesions. Work is in progress in a number of institutions to develop such a test. Hall, Dowdy, Penn and Bellamy[5] have reported a series of sero-flocculation tests for cancer of the gastro-intestinal tract. They tested 122 cases with proven gastro-intestinal tract cancer and in 93.2 per cent the correct diagnosis was made. The test was incorrect, either falsely positive or negative, in 6.8 per cent of the cases.

Continued effort along these lines may be expected to decrease markedly the percentage of patients considered inoperable when first seen, or found inoperable at exploration.

In recent years the use of more radical surgical procedures has been suggested as a means of improving the survival rate of patients undergoing operation, and the use of total gastrectomy for many of the smaller gastric neoplasms now routinely treated by subtotal resection has been suggested. Until about 10 years ago total gastrectomy was rarely performed and was reserved for the isolated case in which the entire stomach was invaded by a neoplasm but in which distant metastases were thought to be absent. Many of our impressions of the results of total gastrectomy have been formed from the follow-up results of such patients, many of whom developed rapid recurrence of the carcinoma, so that in the minds of many people, the symptoms of recurrent abdominal cancer are confused with the symptoms of total gastrectomy.

With the development of the antibiotics, and improvements of anesthesia and surgical techniques in recent years, it has been possible to lower the mortality rate of this procedure to a point where it compares favorably with that of other types of operative procedures for cancer of the stomach. Statistical proof that total gastrectomy provides a better chance of survival from cancer of the stomach than does a subtotal resection is not as yet available. The present rational for total resection is based largely on theoretical considerations.

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There are five ways in which cancer of the stomach spreads from the initial lesion: (1) by direct extension in the wall of the stomach; (2) through the regional lymphatics, into the regional lymph nodes; (3) by extension into adjacent organs, such as the liver, pancreas, transverse colon or meso-colon or into the anterior abdominal wall; (4) through the blood stream; and (5) by direct seeding or implantation through the peritoneal cavity.

In considering these various methods of spread, there is theoretical evidence that a total resection would offer a greater hope of eradicating the malignant lesion and certain of its primary pathways of spread. It is difficult in many respects to identify a malignant neoplasm of the stomach as an early lesion. The duration of the patient's symptoms may have little to do with whether the lesion is early or not. Some patients with very massive, far advanced cancers and widespread metastases have symptoms of brief duration, while other patients who have had stomach symptoms that might be related to disturbed gastric function for many years may have a small localized lesion without spread.

In a recently reported series of 55 gastric carcinomas treated by total gastrectomy, the lesions were divided into "limited" and "infiltrative" groups according to the gross type of the tumor. Metastases to regional lymph nodes were found in 62 per cent of the "limited" group and in 80 per cent of the "infiltrative" lesions.[6]

Coller, Kay, and McIntyre[7] found that it was impossible to tell without microscopic section whether the lymph nodes were invaded by metastasis unless they were obviously completely replaced by carcinoma. They found no relationship between the duration of symptoms, nor the size of the neoplasm and the extent of lymphatic metastasis.

One of the most common pathways of lymphatic spread is along the vessels of the lesser curvature of the stomach and the left gastric vessels down to the celiac axis. A second common pathway of spread is into the duodenal or pyloric lymph nodes. Other glands which are less frequently involved are those along the course of the greater curvature of the stomach, the splenic nodes, and the lymph nodes about the lower end of the esophagus.

It is also difficult to determine the limits of the neoplasm in the stomach wall at the time of operation. Coller, Kay and McIntyre reported that the upper margin of the neoplasm could not be determined at operation by palpation alone in 24.5 per cent of the cases. Mr. Headley Adkins has described the presence of malignant cells in the upper margin of the surgical specimen following subtotal gastric resection in 18 of 19 cases studied.

Extensive metastatic peritoneal implants or distant blood borne metastases obviously preclude eradication of the neoplasm by any type of resection; however, certain direct extensions of the carcinoma outside of the stomach wall may be included in the resection if aggressive surgical principles are adopted. Resection of involved portions of the pancreas, esophagus, colon, and liver may at times be indicated.

Operative technique for total gastrectomy: The abdominal approach is usually preferred. The greater omentum is removed from the transverse colon so as to include all of the lymph nodes along the greater curvature and any possible neoplastic implants that might be included in the omentum itself. The gastro-epiploic and right gastric arteries are divided at their origins and the supra- and infrapyloric lymph nodes carefully removed. Mobilization of the greater curvature is completed by division of the vasa brevia, or, if the spleen is to be included in the resection, division of the splenic artery and vein. The stomach is reflected upward. The left gastric vessels are visualized and divided in the retroperitoneal area and lymph nodes about the coeliac axis removed.

Weinberg[8] has recently proposed the injection of a dye, pontamine sky blue, into the wall of the stomach when the operation is started. This dye is dispersed into the regional lymphatics, staining the nodes a blue color, so that they are much more easily identified at the time of operation. A peritoneal flap which starts from the gastrohepatic omentum and extends across the esophagogastric junction to the left side of the diaphragm is then elevated and the vagus nerves divided. The wall of the esophagus is visualized but is not thoroughly cleaned. No attempt is made to free the esophagus up through the diaphragm.

The preferred anastomosis has been the end-to-side retrocolic esophagojejunostomy, using an inner row of interrupted catgut sutures and an outer row of interrupted fine silk sutures. The peritoneal flap is sutured over the anastomosis to the jejunum. An entero-enterostomy between the two limbs of the jejunal loop is recommended.

An end-to-end esophagoduodenostomy may at times be indicated if the structures can be approximated without tension.

The operating mortality for total gastrectomy has been recorded in several recent reports as approximately 10 per cent.

A nasal tube through the esophagojejunal anastomosis has not been used.

Postoperative care: Penicillin and streptomycin are given routinely for the first week after opera-

tion. Parenteral feedings are given for 48 hours. If the patient's general condition is satisfactory at this time, small amounts of water are given by mouth. This is slowly increased until the patient is taking a full liquid diet by the fifth or sixth day. The majority of patients will then tolerate a soft solid diet in six small feedings. A high protein, high carbohydrate, low fat diet in frequent small feedings supplemented with vitamins and ferrous iron, is prescribed on discharge.

A transient diarrhea lasting two to three days has been observed frequently when soft solid foods are started, but, in no instance, has this persisted.

Follow-up results: In a previous report,[6] we summarized the pertinent data on 11 individuals who were alive 12 months or more after total gastrectomy. The longest survival time in this series was 54 months. All but three patients had made satisfactory gains in weight. The majority had good appetites and six of the 11 had normal food capacities. The remainder were still eating four to six small meals a day and had limited capacities. Only two of the 11 patients had no gastro-intestinal symptoms either during or after meals. The majority complained of some degree of epigastric fullness and discomfort with or without associated heartburn at the time of, or shortly after meals. All of the patients had normal bowel habits and none of them were troubled with diarrhea. Recent blood studies had been performed on all cases and in no instance was there anemia. A majority of patients were working regularly and had been able to return to their normal occupations.

A second study has been made of eight patients who have survived total gastrectomy for 22 months or more. Seven of these patients have lived from 22 to 29 months following total gastrectomy and one patient has survived seven and a half years.

None of the patients showed evidence of metastasis. In all cases an end-to-end esophagojejunal anastomosis was performed. The observations have been grouped into three chief categories: (1) general health and habits; (2) blood studies, both hematological and chemical; (3) digestive and metabolic studies.

General Health and Habits

At the time of our observations six of the patients were in good general condition. They were eating well, their strength was good, they were able to perform their usual work, and they seemed well satisfied with their general physical condition.

One patient operated upon elsewhere seven and one-half years previously had led a normal life until the onset of symptoms of a severe macrocytic anemia about three months before her recent admission here.

The only patient whose postoperative course has been consistently unsatisfactory is a 68-year-old man from whom an extensive benign gastric lesion was removed 25 months prior to this study. He has complained of epigastric fullness and generalized abdominal cramps after eating even very small amounts. He lost seven pounds in the first six months after operation and has failed to gain since that time. His general condition at the present time is fair. For lack of a better explanation, after complete examination, we have been forced to conclude that he is one of a small group of patients whose digestive systems do not become satisfactorily adjusted to the absence of the stomach.

Hematology

In one patient, as stated, there developed a severe macrocytic anemia with subacute combined degeneration of the spinal cord approximately seven and one-half years after total gastrectomy. Before operation her red blood cell count was normal and her hemoglobin slightly below normal. At the time of our recent studies the red blood cell count was 1.8; hemoglobin, 7.0. The mean corpuscular volume was 128 cubic microns.

All of the other seven patients had mild anemia and in two there was a slight increase in the mean corpuscular volume, although this was not considered significant. None of these patients has taken ferrous iron as regularly as has been advised, and it is not surprising that a mild degree of anemia is present.

Blood Chemistry

Studies of the nonprotein nitrogen, sugar, chloride and carbon dioxide combining power show little variation from normal. Various values that were determined to demonstrate liver function showed no evidence of severe impairment in any of the patients. The serum bilirubin was slightly elevated in four patients. The prothrombin time was significantly prolonged in three patients.

Digestive and Metabolic Studies

X-ray studies after ingestion of barium show the esophagojejunal anastomosis to function satisfactorily and the activity of the intestinal tract to be normal in all patients. Jejunoscopy of all these patients, in some instances, showed the rugae to be slightly thickened. There is no evidence of dilatation of either jejunal loop or of scarring about the site of the anastomosis.

Protein Metabolism

The digestion of proteins was investigated in two patients. In the first patient the fecal nitrogen was slightly elevated. The second patient showed a stool nitrogen output of more than three times the normal

value. It is interesting that both of these patients on the original diets were in slight negative nitrogen balance.

Fat Metabolism

Four patients were placed on a diet of calculated fat content and subsequently the quantity of fat in a 48-hour stool collection was determined.

The fat content of the stool was normal in two cases but greatly elevated in the other two.

In two other patients the percentage of fat of the dry weight of the stool was found to be elevated while they were on an uncalculated diet of their own selection.

Carbohydrate Metabolism

The carbohydrate metabolism was investigated in six patients by means of oral glucose tolerance tests. There were, of course, individual variations, but the following generalizations may be made:

(1) All fasting blood sugar determinations were within normal limits.

(2) The peak of blood sugar concentration in all patients was distinctly above normal and was delayed in most cases.

(3) There was also a definite delay in the return of blood sugar concentrations to normal.

(4) None of the patients had a significant hypoglycemia following the initial blood sugar rise.

From the apparently conflicting data that has thus far been collected in this and other studies, certain definite conclusions concerning gastrectomized patients may be made. Other very important facts remain uncertain and can be answered only as additional experience is accumulated.

The following facts at the present time seem well established:

(1) The majority of patients, if free of metastasis, are able to return to a normal mode of life. They gain weight, although frequently the gains are small. Their appetites and bowel habits are normal and they are able to resume their usual occupations.

(2) Anemia develops soon after operation but may be corrected by an adequate intake of ferrous iron.

(3) Usual blood chemical values are within the normal ranges.

(4) Liver function remains adequate.

Other observations requiring further investigation before their final evaluation are the following:

(1) There is a wide variation in the ability of these patients to assimilate the dietary protein and fat. The majority of the patients excrete normal amounts of unabsorbed protein but excessive quantities of fat. At present these variations, however, cannot be correlated with the clinical course of the patients in the limited group studied.

(2) The abnormalities of the glucose tolerance curves of the patients observed by Farris, Ransom and Coller[9] were considered a result of rapid glucose absorption from the intestine. The abnormalities consistently demonstrated in the present series cannot be explained on this basis. Additional studies on this phase are indicated.

(3) The total number of patients who have survived total gastrectomy for over five years must be small. Up to 1943 only 16 patients were known to have lived over three years. At least three authentic cases of macrocytic or pernicious anemia (including the case in this series) are known to have developed more than five years after operation. What percentage of gastrectomized patients will develop this late complication is unknown.

(4) There is suggestive evidence that there may be a small number of patients whose bodily functions do not become satisfactorily adjusted to the absence of the stomach.

Summary

The postoperative courses of patients following total gastrectomy seem to fall into one of four groups:

(1) The occasional patient experiences little or no digestive distress after operation and within a few weeks is taking an almost normal diet with ease.

The remaining patients suffer mild to moderately severe digestive adjustments, which may follow any one of the three courses described in the remaining groups.

(2) Digestive symptoms merge with the symptoms of early recurrence and the patient dies without ever having fully recovered from operation.

(3) Digestive symptoms grow progressively less disturbing and in six to 12 weeks the patient resumes a fairly normal dietary and work regime.

(4) There is a rare case in whom persistent digestive complaints weaken the reserve of the patient to a point where slight additional nutritional interference may cause an unexpected death.

From theoretical considerations a block resection of the entire stomach and regional lymph nodes would seem to offer the best chance of eradicating a malignant gastric neoplasm. Actual statistical evidence that total gastrectomy produces better five-year survival rates than sub-total gastric resection is not at present available.

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7 CANCER
Danger Signals

1. Any sore that does not heal.
2. A lump or thickening in the breast or elsewhere.
3. Unusual bleeding or discharge.
4. Any change in a wart or mole.
5. Persistent indigestion or difficulty in swallowing.
6. Persistent hoarseness or cough.
7. Any change in normal bowel habits.

The Use of Radium in the Treatment of Endometrial Cancer

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Carcinoma of the endometrium presents a different set of circumstances, and different type of behavior than does carcinoma of the cervix. One of the main distinctions between the two is the favorable curability of endometrial cancers. That has been attributed to tendency for the tumor to remain within limits of the myometrium. Many years ago the College of Surgeons collected statistics to establish the average curability for the disease in operable patients and arrived at a value of somewhere between 60 and 65 per cent. Since that time, other series of collected statistics have established for the ordinary simple hysterectomy a survival rate of the same order.

Obviously all patients are not operable. Endometrial cancer occurs in an older age group. It is associated rather intimately with diabetes, cardiovascular disease, and obesity. All of those factors contribute to inoperability in some patients even though they present what appears to be an early lesion, and present a tumor that is believed to remain for long periods of time within limits of the myometrium itself.

Due chiefly to work contributed by Heyman, considerable experience has been gained in the treatment of endometrial cancer with radiation. With gradual improvement in clinical results the method was extended to operable patients. Statistical values have been obtained that equal the results obtained from hysterectomy alone.

About 15 years ago, we began at the Barnard Hospital a program of pre-operative radiation in the operable cases of endometrial cancer. That program subsequently became a routine procedure and has extended also to the patients at the Barnes Hospital. A review of that experience may help establish some facts upon natural history of the disease and some rationalization for treatment.

Endometrial cancer has a tendency toward invasion of the cervix. Extension of the tumor in that direction opens pathways for spread available to cervical cancer. The prognosis is impaired, and most authors consider cervical invasion as evidence of inoperability for endometrial cancer.

Prognosis is affected also by size of the uterus. With uterine enlargement there is a lesser survival rate than for patients with uteri of normal size. An exception to that rule is to be noted for methods of radium treatment patterned after the "packing" method described by Heyman. Filling the uterine cavity with radium tubes provides a more uniform method of distribution and is a method essentially independent of uterine size.

Microscopic appearance of tumor also has a close relationship to end results. The prognosis in well-differentiated forms is much better than for anaplastic varieties. One might expect the undifferentiated tumor to be more sensitive to radiation, but it is that variety which is apt to be found persistent in gross specimens removed after pre-operative irradiation.

Persistence of tumor in the uterus after pre-operative irradiation is evidence of poor prognosis. The five-year survival rate for those patients is on the order of 45 per cent. Among patients in whom no evidence of residual tumor is found the survival rate is on the order of 80 per cent.

The amount of pre-operative irradiation and the plan of treatment is obviously related to tumor effect. Radium applied as an intra-uterine tandem will result in destruction of tumor in only about 50 per cent of patients so treated. Packing the uterus with multiple capsules of radium results in disappearance of tumor in about 75 per cent. For 100 patients treated by the latter method we may expect to find residual tumor in 25 uteri, with survival of 45 per cent of those patients, or a total of 11. Of the 75 patients showing no residual tumor, there is to be expected an 80 per cent survival, or a total of 60. Thus, 71 patients of the original 100 should be alive and well five years after treatment. That may appear to be a small gain over the survival rate of 60 per cent to 65 per cent for hysterectomy alone, but any gain in survival rate for cancer is important.

The plan of treatment can be divided into two classes, depending upon the performance of hysterectomy. In all patients treatment is begun with x-rays, but if the patient is suited to hysterectomy the amount of x-ray employed is only half to two-thirds that used in the treatment of cervical cancer. Larger amounts of x-ray can be employed if treatment is to be by radiation alone.

Following completion of x-ray the uterus is treated by packing the cavity with multiple tubes of radium. Additional sources are also used in the vagina. A single radium treatment is used if hysterectomy is to be performed later. The dose per tube is on the order of 500 mgm hours radium radiation,

but where a large number are employed it may be possible to decrease the contribution from each source. Hysterectomy is performed as soon as an operation of that magnitude is considered practical. If delay is longer than six weeks there is opportunity for recovery and renewed growth of tumor not destroyed by irradiation. The usual interval is about three to four weeks.

Patients not to be treated surgically are given two separate applications of radium about seven to 14 days apart. For that fractionation there is increase in the total dose that can be given. The uterus is sometimes of smaller size at the time of the second application.

Cancer of the Head and Neck Including Cervical Lymph Node Dissections

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The subject this afternoon, namely cancer of the head and neck, has always been a most interesting one. I have worked in this field many years. I had the good fortune of working with some of the outstanding cancer surgeons in New York City at the old New York Skin and Cancer Hospital. The hospital was founded in 1882 and was the oldest institution in the United States to be founded for the treatment of diseases of the skin and cancer. There is no question but that our merger with the Post-Graduate Medical School of the New York University-Bellevue Medical Center will be a great step forward.

For the last 30 or 40 years the surgeons who preceded us in cancer work were tremendously interested in the two types of cancer that we see so much of in the head and neck, namely the basal cell carcinoma and the squamous cell carcinoma. Let us remember that the squamous cell carcinoma, as Dr. Curtis showed us so beautifully yesterday, is the type of carcinoma that metastasizes readily along the lymph vessels to the regional lymph nodes. The basal cell carcinomas do not metastasize. As they grow and spread they will invade the surrounding structures, and unless removed or destroyed 100 per cent will unquestionably recur and cause further damage.

We have been trained to look upon squamous cell carcinoma of the head and neck the same as we look upon cancer of the breast, malignant tumors of the extremities, cancer of the lung, the esophagus, the stomach, the pancreas, the gall bladder, the colon, or any place in the body where cancer can occur. We think of the primary tumor and the regional lymph node field in the attempt to eradicate this disease. Therefore, at our hospital, for the past 30 or 40 years, especially under the guidance of the late Dr. George H. Semken, who wrote the splendid chapter in Nelson's Loose Leaf Surgery on surgery of the neck, we have almost routinely performed what is known as a prophylactic lymph node dissection. In cancer of the breast, and elsewhere in the body, we know that it is almost impossible to tell by physical examination whether there are microscopic cancer cells present in the regional lymph nodes. Therefore, we feel that in cancer of the head and neck of the squamous cell type the malignant cells may drain into the regional lymph nodes. Therefore, the regional lymph nodes are a part of that cancer field, just the same as they are anywhere else, and should be removed surgically before one finds a large lymph node in which one can easily prove that there is a metastasis.

Just a week before I came here I saw a man in our tumor clinic at Bellevue Hospital who had undergone an operation for a small carcinoma of the lower lip two years ago. He had a small scar one centimeter long with no evidence of local reappearance. It was a beautiful result. When he presented himself in our tumor clinic he had a swelling under his jaw attached to the periosteum of the mandible measuring two and a half centimeters in diameter, a direct metastasis from the carcinoma of the lip. If this patient had had a prophylactic lymph node dissection two years ago, perhaps only a suprahyoid one, being a lip case, including the submental, the submaxillary and carotid nodes he would not have presented himself to us with a large metastatic tumor adherent to the mandible, necessitating resection of the mandible. Therefore I will show you some lantern slides with which I can point out some of these facts.

You see in the work that was done in 1899 and 1900 by Dorendorf and Most that the lymphatics from the lip and from the mucous membrane of the mouth drain into the submental lymph nodes, and in the midportion of the lip they drain to both sides, and you see the lymph nodes in the submaxillary triangle and especially the node that lies on the jaw along the external maxillary vessels. The drainage then passes in front of and across the jugular vein into the chief node lying over the jugular vein and then to the posterior digastric triangle and down the posterior cervical chain region to the supraclavicular fossa. On the basis of this knowledge of lymphatic drainage and the exact location of those lymph nodes, operations have been devised for the removal of those lymph nodes.

If one is going to wait until there is a palpable lymph node that you prove by aspiration biopsy to contain metastasis then you must do a complete block dissection right down to the clavicle, with the removal of the sternocleidomastoid muscle and of the internal jugular vein. If, however, you are going to do a prophylactic lymph node dissection and remove those lymph nodes before you have proven carcinoma in them, you can accomplish this accord-

ing to the technique that has been so beautifully worked out by the late Dr. George H. Semken and described in Nelson's Loose Leaf Surgery.

In this operation you do not have to resect the internal jugular vein, or remove the sternocleidomastoid muscle, but you take the entire sheath of the jugular vein as you do in the axilla or as you do in the groin dissections. The lymph nodes are attached to the sheath of the vein and come away with the sheath of the vein. You remove the fascia of the sternocleidomastoid muscle and preserve the spinal accessory nerve, and you can do this dissection on both sides of the neck without much deformity and no danger of disturbance of venous circulation and with no reappearance of carcinoma in the field.

The incision that we use in our clinic is the incision that Dr. Semken devised, and if you do a complete dissection you add the curve (de Quervain) outwards. This lays open the entire neck so that you can do the dissection all the way from the mandible down to the clavicle. You see where the upper flap is reflected upward without the platysma; the course of the lymphatics passes through the platysma muscles into the submaxillary and submental regions. Down below you can leave the platysma attached to the skin flaps. Here you see how the submental triangle has been cleaned out completely and the submaxillary triangle, the external maxillary vessels ligated on the mandible and that is where the very important lymph node is situated. The external maxillary vessels are ligated at the posterior belly of the digastric muscle and the duct of the submaxillary gland where it passes under the mylohyoid muscle. Here you see the field at the end of the dissection, and when you do a prophylactic lymph node dissection, before there is cancer in the field, especially in lip cases, you can stop at the level where the omohyoid muscle crosses the jugular vein. You do not have to do the supraclavicular lymph node dissection unless the histological examination shows cancer above. In that instance you immediately go ahead in a couple of weeks and complete the supraclavicular lymph node dissection. This slide shows the jugular vein completely freed of its sheath with the lingual vein and the superior thyroid vein coming in here.

The wound is sutured with a small drain in the submaxillary region and a small drain in the posterior cervical space. This is a specimen from one of these prophylactic lymph node dissections, and here again, as in the breast cases with the axilla, we mark the lymph nodes at the lower pole of the parotid with one black silk marking thread, two black silk marking threads at the omohyoid lymph nodes, three black silk marking threads at the posterior digastric region behind the posterior belly of the digastric, four threads at the submental lymph nodes. Here are the submaxillary lymph nodes with the chief node, and here the lowest limit of the posterior cervical dissection, which is marked with six threads. The pathologist separately reports the lymph nodes taken from those different regions. We will then know whether we have to go ahead with the dissection on the opposite side or whether we have to do a supraclavicular lymph node dissection.

If you do a supraclavicular lymph node dissection, as for instance in some cases of breast carcinoma or other lesions, then this is the incision that we use, and this is the field at the end of the operation where you see the internal jugular vein joining the subclavian vein, the thoracic duct entering at this junction and the phrenic nerve running on the scalenus muscle. This is the specimen as it appears with the platysma at the completion of supraclavicular lymph node dissection.

These are some lesions of the lip. I show this one in differential diagnosis. It is a chancre of the lower lip. Never fail in any tumor case of the head and the neck to think of routinely doing a Wassermann examination. It will help you out of many embarrassing situations.

This is a man with a carcinoma of the lower lip which goes as far as the midline. I was very interested to hear Dr. Curtis say that they used to do prophylactic lymph node dissections at Ann Arbor but they do not do them any more. We still do them. Dr. Robert H. Kennedy of our clinic has studied the cases of cancer of the lower lip. He found, in our clinic, that even when lymph nodes in the neck were not palpable, in 14 per cent of the cases there were metastatic lymph nodes found at the time of prophylactic lymph node dissection. In tongue cases, 39 per cent metastatic lymph nodes were found even though the lymph nodes were not palpable. In our clinic we use V-excision and at the time when we do the V-excision perform one side of the prophylactic neck dissection.

Here you see the specimens removed from this patient. He had a bilateral prophylactic neck dissection because the cancer involved the middle third of the lip, and we know that this location drains to both sides of the neck. These dissections were done two weeks apart. Here is this patient after the operation of the V-excision with the bilateral lymph node dissections. He lived for 18 years without any further trouble. We did not have to worry about him even if he did not come to follow-up clinic. We know he would not come to us with a big lump on his jaw as the man I told you about at Bellevue Hospital within the past 10 days.

This is a patient with an extensive carcinoma of the entire lower lip. I always like to say what Dr.

William Worral Mayo said, the father of Dr. Will and Dr. Charlie, "Any cancer that comes toward you is not as bad as a cancer that goes away from you." These fungating tumors are not as bad, do not metastasize as early as the infiltrating lesion. This man was operated on by a modified Dieffenbach cheiloplasty according to technique devised by Dr. Semken. A bilateral lymph node dissection was included and he has stayed well. It is about 18 years since the operation, and there is no further trouble. Here you see him from the side, a little Thiersch graft in here, and here you see the scar going down the neck, due to the bilateral lymph node dissection.

Here is another case which was treated in a little different manner, where a pedicle flap was swung to form a lower lip. This is a man, similar to the one at Bellevue Hospital, who had a little lesion at the angle of his mouth treated by radium. The radium cured that carcinoma of the lower lip, but he did not come in for follow-up. In a big city like New York we do not have enough social workers nor do we have enough money to follow the patients who move sometimes every year from one place to another. He had been treated by radium elsewhere. When he did come to us all of the lymph nodes in the neck were full of metastatic carcinoma. If he had had a prophylactic lymph node dissection at the time of the radium treatment he would not have lost his life the way he did.

As far as carcinoma of the tongue is concerned Küttner showed that there is a decussation of the lymphatics along the median raphé of the tongue, and the lymphatics then go down past the lower pole of the tonsil into the neck. Therefore in every tongue carcinoma the cancer field includes the entire lymphatic field on both sides of the neck. If you want to try to arrest the disease you have to do a bilateral lymph node dissection and that dissection has to go from the mandible down to the clavicle on both sides because the lymphatics of the tongue, decussating, go through the hyoglossi muscles and can go right down along the omohyoid muscle into the supraclavicular fossa, skipping the nodes that lie over the jugular vein area. In the lesions in the posterior third of the tongue they are more apt to go to the chief node over the jugular vein first. When the lesion is in the anterior third of the tongue the lymph nodes that may be involved first may be in the supraclavicular fossa, whereas in the floor of the mouth and the posterior third of the tongue the nodes that lie over the jugular vein are the ones that are first involved.

This is a case of leucoplakia of the tongue. Dr. Curtis showed you in beautiful Kodachrome slides yesterday that leucoplakia of the tongue is a precursor of cancer.

Here you see a lesion that we must never forget, and that is tuberculosis of the tongue. In tuberculosis of the tongue you always have the symptom of pain. In this slide you see a typical carcinoma of the tongue. It does not matter much whether you treat carcinoma of the tongue by irradiation or by surgery. The primary lesion must be arrested first. Then one has to perform a bilateral lymph node dissection from the mandible right down to the clavicle on both sides of the neck in two stages. Dr. Morrow of our clinic studied these cases and found that in 39 per cent of tongue cases when you could not palpate lymph nodes, lymph nodes were, however, involved. In 52 per cent, if you palpated lymph nodes, those lymph nodes not only showed hyperplasia but they were involved by carcinoma.

As far as carcinoma of the soft palate is concerned, one may be able to remove it by surgery. If the lesion involves the tonsil or the base of the tongue, then there is no question but that irradiation is the better method of treatment, but you will also want to perform a lymph node dissection.

This is a man who had a small lesion in the floor of his mouth. He was an old man. He had had two coronary attacks, and we excised the floor of the mouth. On histological examination we found that the lesion was an infiltrating malignant lesion. Therefore, secondarily, we removed the floor of the mouth with the cauterized area of our previous operation in continuity with a complete lymph node dissection, dropping the floor of the mouth into the neck. You see here the final result with the skin of the neck drawn up under the mandible. He stayed well for four years, then he went to France and we lost track of him. He was a Frenchman, and we heard some years later that he had died.

In extrinsic carcinoma of the larynx, it has been our custom to perform a total laryngectomy with a bilateral lymph node dissection at the same time. Here you see the specimen of this patient who has now been alive for 28 years. A Gluck type of tracheotomy was done. There has been no reappearance of the carcinoma. If it is an intrinsic lesion you can just do a laryngectomy without lymph node dissection at the same time, and do the node dissection secondarily.

Now here you see a case of a patient who had a lesion on the inside of her lip. She had had a recent severe coronary occlusion. She had had intensive x-ray treatment for epilation purposes 15 years before, and, on the basis of that irradiation dermatosis, she developed this carcinoma. It grew like wildfire, and it not only grew from inside the mouth on the gingival surface, but it grew out to the surface of the skin. In spite of the fact that the medical men said she was an exceedingly poor surgical risk, we

operated on her and resected the mandible with the tumor and you see the inside of the specimen here with the carcinoma on the gingival surface, and the mandible. Here you see the patient after the operation with plastic repair by a modified Dieffenbach cheiloplasty. In this instance we did not do a lymph node dissection because she was such an exceedingly poor surgical risk. This was done about a year ago and her condition is fairly satisfactory.

Here you see a lesion on the inside of the cheek. It is a fungating tumor and in this type of case you can excise the tumor inside the cheek, and in a lesion like that of low grade of malignancy, you can put a thick split graft on the inside of the cheek. But in other cases like this old man you can see the tumor adherent to the skin. This man was 80 years old. In this instance we had to excise the large tumor which we excised with the angle of the mouth and the skin to which the tumor was adherent. Here you see the inside of the cheek with this large fungating tumor. Two weeks later we did a lymph node dissection and he lived to be 89 years of age. The cheek and angle of the mouth were repaired by sliding a large cheek pedicle flap forward.

This is a case where we removed a tumor of the parotid which we thought was a mixed tumor. Mixed tumors of the parotid may degenerate into carcinoma and it is sometimes exceedingly difficult to make a diagnosis beforehand. We removed this tumor and found that it was an adenocarcinoma of the parotid. So we went ahead and re-excised our former scar, took out the entire parotid gland in continuity with a lymph node dissection. This man lived for 17 years, and here you see him about 10 years after the operation. He died 17 years later from a carcinoma of the prostate, having been admitted to another hospital in New York, and we were able to obtain an autopsy report on him.

Here is a man who had a cancer on the inside of his cheek. A radical procedure was performed, in which we excised the inside of the cheek with overlapping skin and did a complete dissection down to the clavicle in continuity. All of the lymph nodes were involved. He lived for four years and then died from a hemorrhage from the internal carotid artery. We obtained an autopsy on him and there was a metastasis way back in the upper part of the pharynx. Here is the patient after the operation. He lived for four years.

This is a specimen of a carcinoma of the maxilla in which the entire maxilla was resected. It is a very simple and easy procedure, with an incision that is made down along the nose and through the mid-line of the upper lip. A large skin flap is reflected and the maxilla resected. The cosmetic result is good.

This chauffeur was burned on his cheek with a cigarette. He developed an intractable ulcer. He read in the newspaper about some caustic paste that would cure cancer. So he put caustic paste on the ulcer and this is what the caustic paste did. When he came into our hands a couple of years later, this is the way he looked, with a large ulcer and the maxilla exposed. We took biopsies along the edge.

Talking about biopsies, let me digress just a moment. Always biopsy every lesion that does not heal. If you do not get a positive report and suspect cancer, repeat the biopsy and take a sufficient amount of tissue at the margin of the lesion.

Here you see the tumor that was excised. We then took a pedicle flap from the forehead and swung that forward. Three weeks later the pedicle was divided and returned to the forehead. Here you see him after that operation. We followed him for four years and he had no further trouble. He then went down to Maryland and we lost track of him. When he came back during the fifth year, he had a small perforation near the nose. When we examined the inside of the lip he had a reappearance of the carcinoma. We told him we had to do a very extensive operation.

We first prepared a flap on the one side of the cheek, and another flap on the other side of the cheek, and sewed them back in place, the so-called delayed flap. Ten days later we excised the maxilla and tumor. Here you see the perforation in the upper lip, and here you see the maxilla. Looking down into the specimen you see the floor of the nasal fossa and the floor of the antrum. On this side you see the carcinoma that had reappeared in the gingival sulcus. Then the two flaps were swung in to form the new upper lip, the larger cheek flap to form the outside of the upper lip and the smaller flap from the other cheek to form the inside of the lip. Three weeks later the pedicles were divided and implanted. Here you see the case completed with the denture in place. It shows how he can open his mouth, having reformed the upper lip by this form of reconstruction surgery. He has remained well 12 years.

Here you see a man who had a baso-squamous cell carcinoma on his cheek which he had neglected. He was an executive of a corporation in New York and he just wore a patch over the lesion. We excised the tumor with the underlying bones to which it was attached. It was repaired by a pedicle from the forehead and he remained well 11 years and finally died with hypertension and a stroke.

This patient had a basal cell carcinoma of the nose. These cases we excise and repair with a full thickness skin graft taken from behind the ear. This is the result with the full thickness flap healed in place.

Here you see another patient with a more advanced lesion on the nose. Here the underlying bone must be removed and the defect repaired by a pedicle forehead flap, a typical rhinoplastic flap repair. We worry about the lesions at the ala of the nose. They are bad actors. We prefer to treat these by radical surgery, to be sure that we have the whole lesion out. We repair the defect by taking a forehead flap from the forehead and cheek flap from the side. Here you see the patient after such a procedure. She remained well for 15 years.

This is an old lady who had radium treatment, elsewhere in New York State, for a similar ala lesion. The radium treatment burned a hole through the nose. However, when we did a biopsy we found that she had a carcinoma in spite of the extensive radium treatment. So here we have the specimen. You can see how the carcinoma has grown into the floor of the nose. It required excision of a portion of the maxilla, and we repaired that by taking a flap from the forehead to form the side of the nose, a cheek flap swung forward to form the upper lip. Here the occluding denture is in place. If you have removed so much of the maxilla some of the dentures will not stick to the remaining palate, even with stickum. Then the orthodontist must make a plate like this one, with two springs on either side which will hold the upper plate against the perforation that goes from the mouth into the nasal cavity.

In this case you see a patient with a lesion on the side of the nose infiltrating the inner canthus of the eye and extending into the orbit. It was adherent to the bone and we knew that we had to do a wide excision with an exenteration of the orbit in order to arrest that disease. This is the specimen, with the eye of the exenterated orbit, the side of the nose, the side of the cheek with the outer wall of the maxilla, the nasal bone, and the ethmoid cells. The defect was repaired with a flap taken from the forehead. This operation was done 27 years ago and I hear from her every Christmas. She lives in Pennsylvania and she sends a Christmas card stating she has had no further trouble.

This is a very old lady who has had many operations for basal cell carcinoma of the cheek. She had also had intensive x-ray treatment. She had one of those infiltrating basal cell carcinomas of the side of the cheek and it was adherent to the mandible. She was over 80 but she suffered so intensely that her son, who is a doctor in Detroit, and a daughter, and the patient herself pleaded that something be done. She could not stand more irradiation. So we prepared a long tube flap on the chest, prepared a flap on the chest at the end of the tube, and then excised the entire lesion. You see the specimen consisting of the ear, all of the skin of the cheek, the angle of the mouth and going down onto the neck. Here you see the repair. The ear was removed, and this opening shows where the ear canal is. We took a pedicle scalp flap from the forehead to help close the defect, and this is the tube flap taken from the chest. That was two and a half years ago and she is now 83½ years old, and at least is relieved of the suffering she went through.

This patient is a doctor, a doctor who would not heed the advice given to him by other doctors. He had had intensive x-ray therapy for acne as a young boy and on the basis of radiation dermatitis he developed a carcinoma at the ala of his nose. He then had a lot of radium treatment. He was sent to me to have a reconstruction operation performed because they thought he had a radium burn. He was addicted to morphine as he suffered so intensely. Something had to be done. I felt sure that there was still carcinoma there. We took eight biopsies from the inside of the nose and from various regions of the lesion and in all of them there was a positive biopsy. So here again we had to do a resection of the maxilla, the nose, and the floor of the nose.

To repair the damage which you see here, we did one of Dr. Gordon New's sickle flap repairs. You see here how you prepare the sickle flap in stages, putting a Thiersch graft on the under side of the flap and on the pericranium. Here you see the flap completely prepared, adherent on the forehead and in front of the ear from where it gets its blood supply through the temporal artery. Here you see that flap lifted away with the Thiersch graft healed in place on the pericranium and on the undersurface of the flap. Then you divide the flap at the forehead, implant it into the defect, leave it there for three to four weeks, and then divide the pedicle. The remainder of the flap is returned to the forehead. The implanted flap is allowed to stay until new lymph vessels and venous channels have formed. It is then moulded into shape to form a new ala. Here you see the end result. This operation was performed three years ago. He is a doctor in Elmira, New York, and so far he has had no further trouble and is no longer on morphine. A neck dissection was done for a metastatic cervical lymph node.

This is a hemi-glossectomy performed on a man who was a heavy drinker and a heavy smoker. When it comes to carcinoma of the tongue as Dr. Curtis said yesterday, if the patient has a positive Wassermann, the prognosis is always much more serious. In our clinic was have not had a single case of carcinoma of the tongue, accompanied by syphilis, in which the disease has been arrested for five years. It is a very bad combination. They have all died of carcinoma before five years.

This man had neglected himself. He drank two quarts of bourbon whiskey a day, and with great difficulty, under endotracheal anesthesia, we did a hemi-glossectomy. Here is one of the specimens of the complete bilateral lymph node dissections in which you see the submental, the submaxillary, the omohyoid, the lower pole of the parotid, the crossing across the jugular vein with the chief carotid node, the posterior digastric and the entire posterior deep chain of lymph nodes including the supraclavicular lymph nodes. He had involvement in eight or ten of the lymph nodes on both sides of the neck though no nodes were palpable on examination. He lived for two years. There was no local reappearance, either in his tongue or on either side of the neck, in the operative fields. Then suddenly he was riddled with carcinoma. We obtained an autopsy on him. The autopsy revealed generalized carcinomatosis including his heart muscle, and every organ in his body was just riddled with carcinoma. There was no reappearance in the fields of operation.

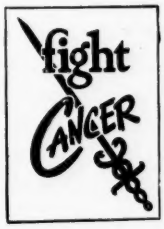
I am eager to show this case because it teaches an important lesson. This is a woman who had a toothache. On account of the fact that she had a toothache she went to a dentist in Washington, D. C., who extracted a tooth. The socket did not heal and he thought she had an infection. Therefore the patient was put on penicillin, kept on penicillin for three months and still the socket did not heal. The socket was curetted several times and "granulation" tissue removed. Finally, at the end of three months, a surgeon in Washington, who was asked to examine the patient, had the important idea, which the dentist should have had long before, that a biopsy should be done because the wound would not heal. A biopsy was done on the tissue from the socket of this tooth, and she had a carcinoma. What had happened was that she had a carcinoma in the antrum which had caused her toothache. The tooth was extracted and the carcinoma then grew down through the tooth socket and presented in the tooth socket. Always be suspicious of a cancer in any part of the body and try to make the diagnosis, as you saw in that beautiful moving picture film of the American Cancer Society this morning—"Early Suspicion, Adequate Diagnosis, and Efficient Treatment."

Here again you see a doctor, one of our former well known anesthetists in New York, who had a lesion under his jaw. He had given anesthesia for innumerable patients who had cancer. Yet he did not think of cancer. A doctor friend in upper New York State, where the patient was on summer vacation, examined him and also did not think of cancer. He went into a clinic in a city up-state and the friend incised the swelling under his jaw under local anesthesia, thinking it was an abscess. He obtained blood and had great trouble in stopping the bleeding. The patient was sent back to his summer home with the wound packed. Four months later, after his vacation, he came to New York. Another doctor treated him with penicillin and then referred him to me. I took him to the hospital. I suspected that it was carcinoma. Biopsy was done within 24 hours and showed that he had a virulently growing ulcerating carcinoma occurring in the submental and submaxillary regions. He had had two coronary thrombosis attacks and he had two hemiplegic strokes and he was really in bad shape. Still we excised the tumor of his neck with the mandible. The specimen shows the mandible and surrounding tissues. The repair of the defect was achieved with a pedicle flap taken from the chest. Well, this dear old gentleman lived for a year and a half and then died of general carcinomatosis. I show you these slides to impress upon you the fact that any lesion that does not heal is more apt to be carcinoma than chronic infection.

This is a man upon whom we did another of these extensive resections of the mandible with a complete lymph node dissection, where again a biopsy had been taken in another good hospital in New York. The biopsy was reported negative. A second surgeon did another biopsy. This biopsy was also reported negative. When we examined the slide of this last biopsy there were tiny minute fragments of tissue on the slide. Let me urge you to take out the whole lesion as the biopsy, if it is a small lesion. If it is a big lesion, then take enough tissue to enable the pathologist to make a diagnosis. Give the pathologist a chance. In this case, an oral surgeon in New York finally performed an adequate biopsy and the pathologist found that in the region of the alveolar margin of the mandible there was a carcinoma growing. Every lymph node in the neck was involved. You see here the resected mandible and the cervicle nodes removed in continuity. We used a heavy dental wire to hold the fragments apart and you see this wire on the x-ray. From the side you again see the dental wire put into the mandible and into the ascending ramus. Usually one repairs the gap later with a rib implant or a section of the crest of the ilium after removing the wire. Because this man had all of the lymph nodes involved we did not do a bone implant. After two years he had a reappearance of the carcinoma and died from it. This cancer could have been diagnosed a year and a half earlier if a sufficiently large biopsy had been taken. This slide shows the man after the operation with the mandible resected. The other side shows the scar of the lymph node dissection. The lymph nodes on both sides of the neck were involved.

Finally, this is the case of a woman who was a heavy smoker. She had a very extensive carcinoma of the buccal mucosa. We had to excise all of the cheek, that is the inside of the cheek, all of the muscles of the cheek, and the only tissue that we could save was the skin of the cheek. In a case like this we make an incision through the lateral portion of the lower lip, turn the cheek flap up, and then take a forehead pedicle flap and turn that forehead flap inside so that the skin of the forehead forms the inside of the cheek. After three weeks the pedicle is divided, returned to the forehead and then the skin of the cheek, which was the only tissue we could save, is on the outside and the skin of the forehead lines the inside of the cheek. Here you see this patient after the operation. We also performed a lymph node dissection. She had metastases in the nodes of her neck. Here she is with her denture in place and with her mouth wide open. You can now see the skin of the forehead lining the inside of the cheek. She has remained well two years so far.

In closing I would like to impress one thing upon you. Dr. Stanley Reimann of Philadelphia has aptly stated, "Unless you remove a cancer 100 per cent the patient is eventually going to have a reappearance of the cancer." Therefore in any lesion suspected to be cancer, especially lesions that do not heal, perform an adequate biopsy, know the complete cancer field—the primary tumor and lymphatic drainage area—and completely and efficiently remove it. Remember the slogan, "Early Suspicion, Adequate Diagnosis, Efficient Treatment."



Bronchiogenic Carcinoma

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Bronchiogenic carcinoma is a very common lesion and is increasing more than any other cancer. It has become one of the most frequent cancers in men. Although it occurs about three times more frequently in men than in women, its incidence in women is also increasing. There has been considerable speculation concerning the cause of the tremendous increased incidence of bronchiogenic carcinoma in the past 25 years. I am convinced that the increased incidence is due to the increased use of cigarettes. There is a distinct parallelium between the incidence of bronchiogenic carcinoma and the sale of cigarettes and there is evidence that tobacco contains substances which are carcinogenic.

Dr. Evarts Graham, whom all of you know, for many years would not agree with me that there was causal relationship between cigarette smoking and bronchiogenic carcinoma. As a matter of fact he used to chide me about my contention and stated that although such relationship exists, there is also a relationship between the increased incidence of bronchiogenic carcinoma and the sale of nylon stockings, which, of course, there is. Relatively recently, Wynham, a young medical student at Washington University, demonstrated in Dr. Graham's own cases, that the incidence of cigarette smoking in patients with bronchiogenic carcinoma is considerably greater than in the hospital and general populations.

We have divided our cases into two groups, those which are resected and those not resected. The incidence is higher in males in both groups; in fact, there is a definite predilection in men. Bronchiogenic carcinoma, as are most carcinomas, is a disease of advancing age, the greatest incidence being in the fifth, sixth and seven decades. However, younger persons are not exempt from the bronchiogenic carcinoma.

We were fortunate in having Dr. Charles Dunlap, the professor of pathology of Tulane, go over all the lungs which have been resected for bronchiogenic carcinoma and classify them according to histologic type and according to the grade of malignancy. It is of interest to see how the histologic type varies with the two sexes. Epidermoid carcinoma is the lesion which is found primarily in men, and adeno-carcinoma is a relatively infrequent type. Undifferentiated tumors occur with equal frequency in both sexes. Adenocarcinoma is the most frequent type found in women. We are of the opinion that adenocarcinomas probably originate in an epithelial rest, or possibly adenomata as Graham and Womack have suggested.

Bronchiogenic carcinoma occurs with about equal frequency in the two lungs, 55 per cent of our resected cases being in the right lung, 45 per cent in the left lung. I would like to call attention to the fact that the upper lobes are involved more frequently than any other part of the lung. This is important for us to know as clinicians because these are areas which are likely to be missed bronchoscopically. I will show you a little later that bronchoscopic examination, although it should be done, is likely not to give a high yield of positive diagnoses, and one of the reasons for this is that bronchiogenic cancers are usually located in the upper lobe bronchi; i. e., they are around the corner and cannot be visualized. Relatively few of them occur in the lower lobe bronchi. Also some occur in the periphery and are not visible. Bronchiogenic carcinoma spreads as do other carcinomas by direct extension through the lymph stream, through the blood stream, and also intra-bronchially. The intra-bronchial extension gives rise to some of the bizarre pictures on roentgenographic plates and must always be kept in mind.

There is one type of extension that I would like to emphasize; that is implantation. As physicians, we are responsible for extension by implantation either as the result of aspiration or as the result of operation. We fear aspiration biopsy because we have seen four patients in whom there was seeding of tumor cells along the aspiration site, and we believe that although this is a valuable method of making a positive diagnosis it shouldn't be used because it may preclude curability.

Lymphatic extension is to the regional lymph nodes. Several years ago Dr. DeBakey and I collected the reported cases of bronchiogenic carcinoma, most of which were observed at autopsy. This study demonstrated that mediastinal lymph nodes were involved in about three-fourths of the cases. Since most of the cases were fatal, the metastases were more extensive than they would be in non-fatal cases.

I would like to call attention to one site of metastases, the skin, which is important because it can be so easily visualized and should always be looked for. Four per cent of our patients had skin metastases. It is imperative in an individual in whom a bronchiogenic carcinoma is suspected that a very careful examination of his entire body be made to determine the presence or absence of skin nodules, because if

they are found one can readily remove one and determine whether the lesion is neoplastic or not. Obviously if there are extensive cutaneous metastases the case is inoperable.

In considering the type of lesion histologically according to age, one sees that up to the age of 50 the three types of carcinoma occurred with about equal frequency, but with advancing age the incidence of epidermoid carcinoma increases and the incidence of adenocarcinoma decreases. If the adenocarcinomas are on the basis of a congenital rest, it is likely that they would occur more frequently in younger people. If the epidermoid carcinoma is due to a chronic irritation over long periods of time, such as smoking, the longer it has been existent, the more likely it is to occur.

The clinical manifestations of bronchiogenic carcinoma unfortunately begin so insidiously that the diagnosis is likely not to be thought of. The most important factor in making a diagnosis of bronchiogenic carcinoma is to think of its possible existence. I emphasize to our undergraduate students that every man past 40 years of age who has an unexplained thoracic discomfort must be considered as having a bronchiogenic carcinoma until proved otherwise. Obviously not all such patients will have a bronchiogenic carcinoma but a large number will and relatively few diagnoses will be missed.

Many patients with bronchiogenic carcinoma have the history of a previous respiratory tract infection such as influenza or pneumonia from which they do not recover as they normally should. Unresolved pneumonia is frequently diagnosed and I am sure that although unresolved pneumonia does occur, it is so rare that one should be hesitant about making the diagnosis. Cough, without a doubt, is the most prominent manifestation that these patients have. However, most persons who smoke have a cough, and because of this it is likely to be disregarded. If, however, the cough changes in character it is of great significance. Hemoptysis always demands investigation as does a persistent thoracic discomfort. Most of us are not conscious of the fact that we have a chest, and if for any reason we do become conscious of it, it demands investigation. Wheezing, which previously had not been present, suggests bronchiogenic carcinoma. It means bronchial obstruction and in a man past 40, who previously was free from the symptom, is indicative of bronchiogenic carcinoma.

The late manifestations are those of complications. Fever is due either to break down of the tumor and production of an abscess or to obstruction of the bronchus by the neoplasm with the development of pneumonitis distal to it. I would like to emphasize that a spontaneously occurring lung abscess, particularly in a man, almost without exception, unless there is a definite story of aspiration or of a frank pneumonia, is caused by bronchiogenic carcinoma. Pain usually means extension to the adjacent structures, i. e., the parieties of the mediastinum. Digestive disturbances in our series have been due largely to involvement of the vagi. Emaciation is a terminal manifestation.

In our series of cases cough was present in 90 per cent, weight loss in 66 per cent, pain in the chest, denoting extension beyond the lung, in 65 per cent, hemoptysis in 57 per cent, previous respiratory tract infection in 53 per cent, etc.

I would like to emphasize that voice change occurred in eight per cent of our cases. There are many thoracic surgeons who are of the opinion that a patient with bronchiogenic carcinoma, in whom there is involvement of the phrenic or recurrent laryngeal nerves, should be considered inoperable. Obviously extension beyond the lung, with involvement of the phrenic or recurrent laryngeal nerves, means that the lesion is no longer limited to the lung, but I do not believe that one is justified in assuming that such a case should not be explored. Sixteen of our patients with evidence of recurrent laryngeal nerve involvement were resectable when they were explored. For the past 15 years we have believed that one is as justified in doing a palliative resection of the lung for bronchiogenic carcinoma as he is in doing a palliative resection of the stomach or of the colon, even though metastases may be present in the liver. Early in our experience we reasoned that palliative resection should be done in order to remove the infected lung and to get rid of the fungating mass which produced the symptoms. I hope to be able to show you that this contention is valid not only because of relief of symptoms but also because of increased longevity.

The diagnosis of bronchiogenic carcinoma is not difficult if one will only think of its possibility. By roentgenography one frequently sees a shadow produced by infiltration by the tumor. There may be obstructive emphysema which is an important early sign. A tumor which will permit air during inspiration to pass the mass but will not permit air to get out during expiration will cause an emphysema. As you know, during inspiration, the bronchi dilate, and during expiration they contract. A tumor not large enough to completely obstruct the bronchus during inspiration will admit air past the tumor into the lung distally. During expiration with the contraction of the bronchus the air is trapped and an obstructive emphysema results. This is an early manifestation and is of importance. If the bronchus becomes completely occluded, the air distal to the point of obstruction is absorbed, and with the pro-

duction of atelectasis casts a massive shadow on x-ray. In some instances, particularly in upper lobe lesions, bronchography is of value. Bronchoscopy is of value and should be done in all instances, not only in an attempt to visualize the tumor which is possible in about only one-third of the cases but also because it frequently demonstrates the extent of the lesion. One can tell whether the carina or trachea are involved.

The most valuable diagnosis in our hands has been the cytologic examination of bronchial secretion. There has been some considerable controversy whether this should be done on sputum alone or whether the material should be obtained by aspiration during bronchoscopy. Obviously if one could make repeated examinations following bronchoscopy this should give a higher percentage of correct diagnoses. In our clinic, sputum examinations have given a higher incidence of positive diagnosis because more frequent examinations are possible. In 80 per cent of our cases, we are able to make a positive diagnosis by cytologic examination of the sputum. Thoracoscopy is of more value from a prognostic than a diagnostic standpoint. We use it when we suspect there might be extension to the parieties. Aspiration biopsy I have already mentioned. I believe that it should be condemned as a diagnostic procedure.

Finally, thoracic exploration is a justifiable method of diagnosis. In the man who, clinically, has bronchiogenic carcinoma and in whom the diagnosis cannot be proved or disproved, thoracic exploration is necessary. It is far better to explore in such an instance than to wait until a positive diagnosis can be made without exploration, at which time it may be too late. (A number of diagrammatic drawings were shown to illustrate the changes in the bronchi and lung which may produce changes in roentgenograms. Also a number of roentgenograms illustrating different bronchiogenic carcinomas were shown).

Bronchoscopically if the tumor is in an area which is visible in the bronchoscopic view it is possible not only to visualize the tumor but also to get a biopsy. On the other hand, if the tumor is in the periphery beyond reach or beyond bronchoscopic view, or if the tumor is around the corner in the upper lobe, bronchoscopy is of little value. In upper lobe lesions, there are two methods which can be used to look around the corner, one by means of an instrument which is like a fore oblique cystoscope, and the other by means of a mirror with a light in the end of it, which permits periscopic vision.

In our 237 cases in which pulmonary resection was done for bronchiogenic carcinoma, there were only 90 in which the bronchoscopic examination gave positive diagnostic results (38 per cent of all the cases). A negative bronchoscopy, therefore, does not in any way exclude a diagnosis of bronchiogenic carcinoma, because bronchoscopy makes a positive diagnosis in less than 40 per cent. The cytologic examination of bronchial secretion and its efficacy depends upon training and zeal and the pathologist. It is essential that a good pathologist who is trained in cytologic diagnosis be willing to spend a great deal of time in these examinations. I know nothing that is more time consuming and more painstaking than this type of examination. By cytologic examination of the sputum we were able to make a correct preoperative diagnosis in 80 per cent of the cases.

There is only one curative treatment of bronchiogenic carcinoma and that is a pneumonectomy. There are a number of thoracic surgeons who advocate lobectomy. We have done only five lobectomies but feel that a lobectomy should be performed only when a pneumonectomy is contraindicated. A lobectomy is not a curative procedure in bronchiogenic carcinoma. I think it is just as irrational to do a lobectomy in treatment of a bronchiogenic carcinoma as it would be to remove a quadrant of the breast in a breast carcinoma. No one would even think of doing that, and I don't think that we should consider lobectomy in bronchiogenic carcinoma as a curative procedure.

On the other hand, in a man in his 70's, whose vital capacity is low and whose differential bronchial spirometry shows that he might not be able to survive a pneumonectomy or be able to get along on one lung, one is justified in doing a lobectomy, which must be considered a makeshift procedure. Only a pneumonectomy permits the satisfactory and complete removal of all the mediastinal lymph nodes.

In a total series of 705 proved cases of bronchiogenic carcinoma, 237 were resected, of which 77.6 per cent were considered as palliative resections. A resection is considered palliative when the lesion has extended beyond the lung with massive involvement of the mediastinal nodes, the chest wall, the pericardium, or the diaphragm necessitating resection of these adjacent areas. In a little less than 10 per cent the lesion was so extensive that it was impossible to ligate the hilar vessels outside the pericardium, necessitating their intrapericardial ligation. In five per cent of the cases the auricle was actually sutured, in a little less than five per cent the major portion of the diaphragm was resected en masse with the lung and in a little over five per cent a major portion of the chest wall was resected.

Of the 705 cases, there were 295 that were obviously inoperable. They had a distant extension beyond the local lesion which wouldn't permit at

least a palliative resection. There were 410 who were considered operable, 42 of which refused surgery. The latter group is a large number, most of which were at the Charity Hospital. Three hundred sixty-eight were explored, 52 per cent of the entire group. Of the 368 that were explored, there were 131 that were found to be non-resectable, and there were 237 that were resectable. Of the group that were explored but found to be non-resectable, 23.5 per cent died within the hospital. Of the 237 that were resected, 21.8 per cent died in the hospital and 78 per cent left the hospital, which is 26 per cent of the entire 705 cases.

You are interested not only in the mortality rate but in what happens to these patients afterwards. Of all the patients in which a resection was done, and this includes all the patients that died in the hospital, the survival rates fell rather rapidly until the second year, when a plateau is recorded. Of all the cases that had been resected, 20.8 per cent are alive at the end of five years. If these resected cases are broken down into curative and palliative groups, there is obviously a good deal of difference. Of the so-called curative resections, 44 per cent were alive at the end of five years.

However, I am proudest of the palliative resections, because most of these, I am sure, would not have been operated upon by the majority of thoracic surgeons. What would have happened had they not been resected? I can answer that partially because we have followed all of our patients, even those in which resection was done. In the non-resective cases, there are three groups: (1) those in whom resection was thought to be possible but the patient refused operation (2) those who were obviously inoperable and (3) those who were considered operable but who at the time of operation were found to be non-resectable. The last two groups obviously are the most extensive. Of the three groups of cases in which no resection was done, no patient lived as long as three years in spite of the fact that in every instance some other type of palliative therapy such as x-ray or chemotherapy of some type, was used. Only 0.8 per cent were alive at the end of two years, and less than five per cent were alive at the end of one year.

The results in the resected cases stand out in contrast to these, in that 20.8 per cent of all the cases resected and 12.5 per cent of cases palliatively resected were alive at the end of five years. This demonstrates without any doubt that palliative resection is justifiable not only to relieve symptoms but actually to prolong life.

Dr. Longmire this morning spoke about carcinoma of the stomach and as he said, based on our present statistics in the better hospitals throughout the country, a patient admitted to the hospital with a diagnosis of carcinoma of the stomach has only a five per cent chance of being alive at the end of five years. Dr. Lee Clark of Texas, several years ago, showed that if one considers all the people with carcinoma of the stomach, many of whom do not get to a hospital, the five-year survival rate is from one to two per cent. Carcinoma of the stomach is a lesion, the frequency of which has been appreciated for a long time. We as a profession are cognizant of the frequency with which carcinoma of the stomach occurs. There is not a physician in this audience who hasn't been impressed with the frequency of carcinoma of the stomach ever since he was a medical student, but most physicians consider carcinoma of the lung a relatively rare disease. Actually it has been rare, but its incidence is increasing in frequency. So it is easy to see why physicians have made diagnoses late in bronchiogenic carcinoma because the relative frequency of it is not appreciated.

If we contrast the results in the treatment of bronchiogenic carcinoma with those in the treatment of gastric carcinoma, it is evident that the former are better. Whereas only five per cent of all the patients admitted to the hospital with diagnosis of gastric carcinoma are alive at the end of five years, eight per cent of the patients admitted to the hospital with bronchiogenic carcinoma survived the five-year period even though over 70 per cent were operated palliatively.

When the profession generally becomes cognizant of the fact that bronchiogenic carcinoma is a common lesion and will think of the possibility of its existence earlier, the eight and a half months delay in the diagnosis of our patients will be decreased and the diagnosis will be made earlier so that therapy can be instituted at a time when the lesion is limited to the lung. The incidence of curative resections should then be high and the percentage of five-year survival should be greatly increased.

In conclusion, I would like to reiterate the fact that bronchiogenic carcinoma is a common lesion. It is becoming one of the most common sites of carcinoma in men. It is a lesion that we must think of in every man past 40 who has an unexplained thoracic discomfort, and once the possibility of its existence is thought of the diagnosis is not difficult to make. There is only one form of therapy and that is a pneumonectomy with removal of the regional lymph nodes, the mediastinal lymph nodes. I would like to again make a plea for doing palliative resections because not only will these patients be relieved of their symptoms but also their lives will be prolonged.

Carcinoma of the Bladder with Special Emphasis On Its Surgical Treatment

R. H. Flocks, M.D.

Iowa City, Iowa

Carcinoma of the bladder is one of the more common cancers. During the years 1932 to 1942, .5 per cent of all the admissions to the University Hospital and five per cent of all the admissions to the Urological Department of the University Hospital were carcinomas of the bladder. Next to carcinoma of the prostate, carcinoma of the bladder is the most common carcinoma seen by the urologist. The following discussion is based upon a study of 540 patients who were seen and treated at the University Hospitals in Iowa City during the period 1932 to 1942.

Since the five-year survival rate of those patients treated early is 55 per cent as compared with five per cent in those treated late, an early diagnosis is of great importance. Although symptomless hematuria is said to be the cardinal symptom and sign of carcinoma of the bladder, many patients do not manifest this symptom and sign at all or only in the later stages. Any disturbance of micturition, any change in the urine may be a manifestation of carcinoma of the bladder. In our series, there have been patients who came to the hospital with a diagnosis of chronic prostatitis or cystitis who later proved to have carcinoma of the bladder. It is therefore a good rule to follow that any patient over the age of 20 who has any disturbance of micturition, should have a cystoscopic examination to rule out carcinoma of the bladder. Early diagnosis makes a tremendous difference in the type of therapy which is to be carried out and in the results to be expected from this treatment.

In addition to early diagnosis, the gross pathology of the tumor is of importance from the point of view of treatment and prognosis. Doctor Jewett of Baltimore in a classical study of patients with carcinoma of the bladder coming to post mortem examination, found that these tumors could be divided into three groups: Group A—the non-infiltrating carcinomas; Group B—carcinoma which has infiltrated into the bladder musculature but not completely through it; and Group C—the carcinoma which has infiltrated completely through the bladder wall and into the perivesical tissues. Whether or not any given tumor falls into Group A, B or C, can usually be determined by a combination of a cystoscopic examination, bimanual palpation under anesthesia, cystographic studies and biopsy studies. When the classification of any given tumor is known, the prognosis is indicated: Of those without any infiltration, approximately 100 per cent are potentially curable; of those with infiltration into the musculature, approximately 85 per cent are potentially curable; and of those where the tumor has progressed through the bladder wall, only 23 per

CHART I

Carcinoma of Bladder

Group A (Jewett) — *100% potentially curable*

167 cases treated by transurethral coagulation, 77% controlled

Cause of difficulty:

a. Multiple tumors with extensive coagulation → infection of upper urinary tract → death

b. Change in character of tumors → death due to malignancy

Correction: When multiple, covering much bladder area so that danger of infection is great,—*divert urine* and do cystectomy or coagulation in dry bladder.

CHART II

Carcinoma of the Bladder

Group B (Jewett) — *86% potentially curable*

249 Cases — *39% controlled*

126	Treated transurethrally	53% controlled
74	Treated transurethrally + irradiation	31% "
13	Treated partial cystectomy	40% "
33	Treated miscellaneous methods	10% "

Difficulties:

1.	Primarily infection—local or ascending	13% (34 cases)
2.	Primarily lack of destruction of tumors	28% (66 ")
3.	Mortality	6% (14 ")
4.	Unfollowed	14% (36 ")

cent are potentially curable. The remainder will already have extention into the retroperitoneal nodes or produced distant metastases. By potentially curable, Doctor Jewett meant that no metastases were present and, therefore, complete removal of the local lesion should produce a cure.

Using this classification as a base line, what have been the results in the 540 patients seen in our clinic during the period 1932 to 1942? These patients were treated before our present means of treatment for urinary tract infection were at hand, and therefore, their treatment was carried out under a certain handicap.

Chart I indicates the results of therapy in the 167 patients who fell into Group A. Seventy-seven per cent were alive and apparently free from tumor five years or more after treatment. Many more of these patients probably would have obtained an excellent result if we had had our modern methods for the treatment of urinary tract infection. Moreover, in some of these, more radical therapy, which is now available, might have produced a definite incidence of salvage.

Two hundred forty-nine of the 540 patients fell into Group B according to Doctor Jewett's pathological classification. Only 39 per cent had a five-year survival as contrasted with a potential curability rate of 85 per cent. One hundred twenty-six of these patients were treated by transurethral resection and coagulation of the base of the tumor, and in this group, 53 per cent had a five-year survival. Seventy-four were treated by transurethral resection followed by intensive irradiation. Only 31 per cent of this group survived five years. Thirteen were treated by partial cystectomy. The reason for this is that most of the tumors are located at the base of the bladder and partial cystectomy does not permit one to do a radical removal of the lesion if it is located in that area. Only 13 of this total group were so located in the bladder that radical removal could be carried out without removing the bladder. Of this group of 249 patients, 34 died primarily as the result of infection which might have been prevented with the use of antibiotics. Sixty-six of these cases died because of inadequate removal of the tumor. It is of interest to compare these results with the results obtained in 100 cases of total cystectomy for carcinoma of the bladder reported by Doctor Marshall of New York. In this group, which apparently fell into Group B, only 26 per cent were alive and apparently well at the end of two years. It is of interest to speculate whether or not the manipulation incident to the total cystectomy did not do more damage by pushing tumor cells into the lymphatics and surrounding veins than was gained by the more radical removal of the bladder and the original tumor, as compared with what might have been theoretically accomplished by either transurethral or suprapubic electro-coagulation. It may very well be that this type of tumor could be more radically destroyed by electro-coagulation avoiding manipulation if bilateral ureteral intestinal anastomosis is carried out to avoid upper urinary tract infection and urinary extravasation. This thus would produce end results superior to total cystectomy and ureteral intestinal anastomosis.

CHART III

Carcinoma of the Bladder

Group B (Jewett) — *86% potentially curable*
Cases dying primarily from urinary tract infection:

Type of treatment	No. of cases	Operative deaths	Deaths from urinary infection in those who survived operation
Transurethral resection	126	6	21 (17%)
T.R. + X-ray	74	0	11 (15%)
Partial Cystectomy	13	2	2 (15%)
Totals	213	8	34

CHART IV

Carcinoma of the Bladder

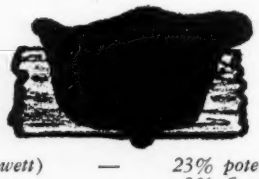
Group B (Jewett) — *86% potentially curable*
Correction:

1. Divert urine and more adequately destroy tumor by total cystectomy or electrocoagulation.
2. Partial cystectomy is applicable in only a small percentage of the cases.
3. Total cystectomy versus electrocoagulation after the urine has been diverted. Invasion of plane of cleavage by tumor.

One hundred twenty-three of this group of 540 cases fell into Case C; 25 per cent of these should have been potentially curable. Only two per cent are alive and free from tumor at the end of the five-year period.

CHART V

Carcinoma of the Bladder



Group C (Jewett) — *23% potentially curable*
123 Cases — *2% Controlled*

12% (14 cases) died primarily of infection
53 treated by transurethral resection with temporary improvement in 69% (35 cases)

Ureterointestinal anastomosis in 3 cases produced excellent palliation. This raises question of its more frequent use + extensive coagulation or irradiation or both in selected cases to raise percentage of controlled cases.

In summary then, the surgical treatment of carcinoma of the bladder is as follows:

1. The destruction of the tumor by means of electro-coagulation either through the resectoscope transurethrally or through an open cystostomy.

2. The removal of the tumor by open surgical procedure, such as partial cystectomy or total cystectomy with diversion of the urinary stream. Any operation, either partial cystectomy, total cystectomy or open resection and electro-coagulation should include the removal of the regional lymph nodes.

3. Palliative treatment in those patients where the tumor itself cannot be removed, for the comfort of the patient. This includes transurethral resection or deep x-ray therapy or diversion of the urinary stream into the bowel.

TABLE I

Emphasis must be placed on:

1. The avoidance of urinary infection:
   a. Antibiotics
   b. Diversion of urinary stream
2. The question of destruction of tumor tissue in plane of cleavage around the bladder:
   a. Removal of portion of rectum
   b. Coagulation with high frequency current — Diversion of urinary stream
   c. Irradiation

Moreover, with regard to cancer of the bladder, the following points should be emphasized:

(a) Early diagnosis is imperative and in any patient over the age of 20, any disturbance of micturition indicates cystoscopic examination to rule out carcinoma of the bladder.

TABLE II

The Surgical Treatment of Carcinoma of the Bladder

I *Destruction of the Tumor by Electrocoagulation*:
   a. Transurethrally
   b. Through a suprapubic cystotomy

II *Removal of the Tumor by Surgical Procedures*:
   a. Partial cystectomy
   b. Total cystectomy and prostate-seminal vesiculotomy
      1. With uretero-intestinal anastomosis
      2. With cutaneous ureterostomy

III *Diversion of the Urine Followed by Destruction of the Tumor by Electro-coagulation, or irradiation, or both.*

IV *Palliative Treatment*:
   a. Ureteral transplantation into bowel / to skin
   b. Suprapubic cystostomy
   c. Transurethral electrocoagulation

(b) Transurethral resection with electro-coagulation of the base and open electro-coagulation of carcinoma of the bladder has a very definite place in the treatment of this lesion. With earlier diagnosis, the vast majority of patients will fall into groups amenable to this type of surgical therapy which avoids manipulation of the tumor, and affords radical destruction of the tumor. By controlling infection either by diverting the urinary stream or intensive antibiotic therapy or both, these methods should yield much better results than have been afforded in the past. In selected cases, radical removal of lymph nodes and lymphatics with total cystectomy and ureteral intestinal anastomosis, is indicated. Palliative treatment consists of ureteral transplantation or transurethral electro-coagulation.

The improvement in the results of ureteral intestinal anastomosis and in the treatment of infection with antibiotics has radically changed the treatment of carcinoma of the bladder in the last three years, making possible more radical destruction of these tumors with great improvement in the results of treatment.

The Present Status of Radiology in the Diagnosis of Curable Cancer

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By curable cancer is meant in general cancer still sufficiently localized to be curable by ordinary surgical or radiological methods, or by combinations of these methods. For practical, clinical purposes, cancer may be subdivided into two main groups, depending on whether it is readily accessible or is inaccessible to ordinary clinical examination.

The accessible cancers are essentially those in five main sites:

skin
lip and oral cavity
breast
cervix
rectum and recto-sigmoid

These are, par excellence, the lesions that can be suspected by the patient fairly early, detected by simple physical examination and cured by prompt, radical treatment. What is the place of radiology in their diagnosis or preliminary care?

In lesions of the skin and early lesions of the lip and oral cavity, it is almost nil. In more advanced oral lesions, especially those of the alveolar ridges, roentgen examination of the maxilla or mandible (for evidence of invasion) and of the lungs (for metastasis) is advisable.

In patients with *breast* lumps, pre-biopsy x-ray examination of the *lungs* and common *bone sites* is strongly advisable. A simple routine of four 14 x 17 films will suffice for most cases: P. A. and lateral chest films with slightly heavy exposure; A. P. and lateral lumbosacral spine films. The yield on bone surveys of other sites (skull and long bones) is so small that it is not economic. The pelvis and hips will usually be adequately visible in the 14 x 17 A. P. lumbosacral film. Needless to say, stereoscopic projections, plus additional studies in the presence of suspected areas in the preliminary films will be advisable in some instances. Repeat x-rays after bowel cleansing may be essential in a few cases. The presence of definite metastatic foci contraindicates radical surgery (Haagensen et al). It is suggested that additional radiological consultation is desirable in questionable cases.

In suspected or definite *cervix carcinoma,* some clinicians request roentgen examination of the urinary tract for evidence of ureteral involvement; the pelvic bones and lumbar spine are visible in these films, permitting detection of bone lesions. However, Heyman and other experienced observers regard the yield as too low to warrant continuation of routine urographic procedures. Indeed, Heyman points out that even though you find evidence of, say, ureteral involvement on one side, you still proceed with roentgen and radium therapy in regular fashion. It is therefore my own practice not to require preliminary urographic examination in cervix cases. Pre-treatment chest x-ray examination is advisable unless the patient has had such in the last year or so.

In most *rectal and rectosigmoid* carcinoma, the lesion is within reach of the examining finger or proctoscope. Indeed, 75 per cent of all cases of cancer of the large bowel are so situated. The incidence of early pulmonary metastasis is low. Should preliminary studies be made? Preoperative chest roentgenograms are probably sound insurance against silent intra-thoracic disease. This would be my own limit. However, some proctologists believe that barium enema studies are worthwhile, since a small percentage of patients with rectal carcinoma also have a second or even third lesion elsewhere in the

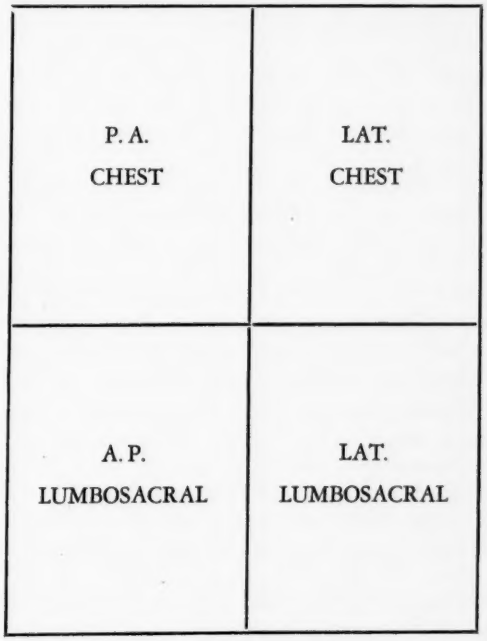


Figure 1. Basic roentgen survey which should be made before operation on or irradiation of breast tumors.

colon. It is certainly agreed that the finding of rectal or rectosigmoid polyps calls for careful single and double contrast x-ray examination of the large bowel.

So much for the accessible cancers... which constitute about 55 per cent of all cancers, and which are curable in most cases by suitable radical treatment, surgical or radiological.

The inaccessible cancers are commonly those of the stomach, intestines, prostate, lung, and other viscera (see Table I).

TABLE I

Incidence of Cancer by Sites (5 most common)
(M. L. Levin, N. Y. State. 1944.) *Per 100,000 population*

Both Sexes		*Males*		*Females*	
Breast	30	Skin	29	Breast	60
Skin	25	Stomach	27	Cervix	30
Stomach	22	Prostate	23	Intestines	24
Intestines	22	Intestines	20	Skin	20
Cervix	15	Lung	15	Stomach	18

In most of these sites roentgen examination is important for early diagnosis. However, as Newell has pointed out, while the value of human life is infinite, funds and time are finite. Can we outline a basic program of reasonable diagnostic radiological procedures for suspected inaccessible cancer? A program which will be practical, irrespective of the apparent source of funds, governmental or private?

Stomach. The incidence of gastric cancer is about 22 per 100,000 population at large. It increases to one per 1,000 in persons over 40 (about one per 700 males and one per 1,200 females). It seems obvious that this incidence is too low to warrant mass detection efforts in unselected groups. If one could select males over the age of 45, who had chemical or other evidence of achlorhydria, perhaps a survey would be worthwhile. However, it is to be recollected that not all persons with silent tumors are willing to part with their stomachs. We are told that in a current gastric roentgen survey of 9,000 asymptomatic males over 50, about seven cases with gastric lesions suspected of malignancy were detected. Only one of these consented to operation: he had a neoplasm, but reportedly developed a fatal pulmonary embolism on the third postoperative day.

Knowing how difficult it sometimes is to detect gastric cancer with the best of fluoroscopic and roentgenographic technique, it is evident that survey methods have considerable limitations. We will therefore confine our further remarks to basic radiological methods in clinical practice. You have a patient, probably over 45, with some symptoms pointing to the upper alimentary tract. What should be done? Careful fluoroscopic examination, spot films for mucosal detail and conventional films for contour and peristaltic records: polygrams in questionable mural lesions: recheck, within two to four weeks, of all small ulcerating lesions or questionable polyps. This upper or partial gastrointestinal study is feasible, economic and useful in the detection of many curable gastric lesions.

We assume that the fluoroscopist always studies the esophagus carefully, as part of his gastric examination: that the lungs and mediastinum are screened, and that the other abdominal viscera are scanned in the conventional films.

Intestines. Small bowel lesions are comparatively rare and will not be dealt with here (see Hodes excellent summary in J.A.M.A.).* Large bowel lesions require barium enema studies, (with added double contrast examination in about 10 per cent of cases). Proper preliminary cleansing of the colon is the key to success. Castor oil, one or two ounces on the preceding afternoon: light supper: no breakfast: cleansing enema if oil catharsis is not complete. Recheck questionable annular filling defects, polyps and ulcers within four weeks.

Prostate. When the examining finger or the history leads to suspicion, make roentgen examination of the lungs and central skeleton as recommended for breast lesions. When bone involvement is present, osteoblastic lesions predominate. However, in bone roentgen studies it must be recollected that extensive invasion may be necessary before roentgen evidence is detectable. Snure showed that 60 per cent of the cancellous tissue of a vertebral body had to be decalcified before a central osteolytic metastasis could be readily seen: much less of the cortex needs to be destroyed to permit detection. Similarly, lung metastases must, as a rule, be three mm. or more in size to be found.

Lung. The incidence of primary lung cancer is reported to be about 16 per 100,000 adults. In males over 45 it is said to be higher. Early detection requires suspicion plus careful roentgen examination. A brassy cough, an occasional tinge of blood call for *not* a survey PA film, *but proper x-ray examination.* No clinician worth his salt would be satisfied with a plain film of the abdomen for the detection of gastric or urinary tract tumors; why try to rely on a single film for the respiratory tract? Fluoroscopy; inspiration and expiration P.A. film; inspiration lateral and oblique films should be the minimum. Supplementary spot films, tomograms, or contrast bronchial studies may be indicated. Sputum and aspiration cell studies, segmental excision and frozen section may be needed to identify the nature of the roentgen shadow.

Other Viscera. The urinary tract (especially the kidneys), the adrenals, the central nervous system

*J. A. M. A. 141, 1284, 1949 (Dec.)

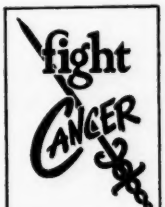
and the osseous system are all fruitful sites for suitable, planned roentgen examination. Time does not now permit their detailed consideration.

Follow Up. Just as early detection of the primary is essential for cure, so is early detection of recurrence or metastasis often essential for prolongation of comfortable life. Some cancers tend to be multiple, notably those of the skin, intestines and ovaries. Periodic recheck of the intestinal tract may yield a second curable lesion and a grateful patient. By and large, periodic bone surveys in the absence of symptoms are not economic. Conversely, symptoms of bone metastasis often deserve treatment prior to their demonstrability. The question of lung surveys is less difficult. A survey film at annual intervals may sometimes yield a solitary curable metastasis. However, I must admit I do not insist upon it, except in patients with intrathoracic lesions (e. g. pulmonary tumors, mediastinal lymphoma, etc.).

Summary. The present day place of radiology in the diagnosis of the common types of cancer is reviewed.

Its usefulness is definitely less than that of ordinary physical examination in cancer of the accessible sites. These are the most frequently curable cancers today.

Conversely, its usefulness is great in the inaccessible growths, notably those of the alimentary, respiratory and genitourinary tracts.



Progress in the Treatment of Cancer

Alton Ochsner, M.D.

New Orleans, Louisiana

I would like to give you a resume of what has been accomplished and what is being accomplished by the American Cancer Society and its activities. I need not remind this audience that cancer is a curable disease. It is just as curable as many other conditions that we have to treat. As a matter of fact, it is more than that. Cancer is preventable.

You here in Kansas, I think, have done one of the best pieces of work that I know, in emphasizing the importance of every doctor's office being a detection clinic. The experiences of the detection clinics throughout the country, and I am sure it is true here in Kansas in your own offices, have been that of the well people with no symptoms at all, approximately one and a half per cent have an unsuspected cancer. That is an important group even though the percentage is low. Almost without exception, these patients have a cancer which is amenable to curative treatment.

However, there is another group which, I believe, is even more important. This is comprised of approximately 15 per cent of individuals in whom a precancerous condition is found. This in itself is of no significance, but if allowed to go on might develop into cancer. The patients in this group, 10 times the number of the actual cancers, if treated correctly can be prevented from having a cancer. The American Cancer Society, in emphasizing the importance of early detection and repeated examinations, is emphasizing a program of prophylaxis which is the desideratum.

Dr. Longmire this morning, in talking of cancer of the stomach, made a plea for earlier diagnoses in the treatment of cancer of the stomach. There is no question that if we are going to improve the results in the treatment of cancer generally, we must get cases earlier. Most cancers can be cured if they are detected early and the proper therapy instituted at a time when the condition is still localized. It is a big fight which we, as an organization, must wage; and the fight is far from won. Conviction of the public that cancer is curable is essential, and in this you women are doing more than anyone else. Physicians cannot do anything unless the people consult them.

There has been, as you know, in the past few years a movement to get the American Cancer Society to participate in a federated fund raising program. It would be fine, I suppose, from a theoretical standpoint, if all of us could donate once a year to all of these projects. However, we, of the Cancer Society, are convinced that it would be detrimental for the Society to participate in such a program for two reasons. First, because during our campaign in April, more is accomplished as regards education than in any other way. If we were to become a part of a federated fund raising campaign the educational value of the cancer campaign would be entirely lost. It is a common observation that during and immediately following the April campaign for funds, more persons consult their physicians for examination than at any other time. Also, if we became a part of federated fund raising, much less money would be raised for cancer because people will give to cancer when they will not give to anything else, and justifiably so.

Although cancer is second to cardiovascular disease as the cause of death, it is more important because it is more amenable to treatment. Far be it from me to decry the importance of cardiovascular disease because I am getting into that age when cardiovascular disease is of importance, but it is largely the result of a wearing out process and we are limited in our efforts to prevent and control it. Cancer, on the other hand, strikes us when we are at the height of our productivity and it is the one principal killer which we are best able to prevent and cure. It is for this reason that the American public is particularly interested in cancer. It is the one killer that we can and must stamp out.

What has been accomplished up to the present time? In surgery, the specialty with which I am most familiar, we are accomplishing a great deal more than we ever did before. We are able to do surgical procedures that we did not dream of before. It is possible now, by the proper preparation of the extremely ill cancer patient, such as the correction of blood volume deficiency which so many of these patients have, to perform operations of magnitudes which were impossible five or 10 years ago. By means of modern anesthesia, operations of almost any length can be performed perfectly safely.

The postoperative care of these patients also is extremely important. This is so important that in our institution we have established a postoperative recovery division to which every patient goes in the immediate postoperative period. We consider the immediate postoperative period one of the most im-

portant phases of the patient's hospital stay. There is no one of us who think of calling the nurses' registry and asking that a special nurse be sent to the operating room to assist in the performance of a complicated operative procedure. Instead we insist upon having a nurse who is not only especially trained in surgical techniques but one who is also particularly familiar with our whims, desires and idiosyncracies. And yet, it is customary to call the nurses' registry for a nurse to take care of the patient in the postoperative period. As far as the patient is concerned, an especially trained nurse in the postoperative period is far more important than such a nurse during the operation because if anything happens during the course of the operation, the surgeon and his assistants are present to take care of any eventuality. On the other hand, after the patient has been operated upon and returned to his room, he is placed under the care of a nurse who may never have cared for such a case and therefore may not recognize early manifestations of a postoperative complication which may mean the difference between life and death of the individual. If ever specialized care is necessary, it is in the immediate postoperative period. I believe the time is coming when every hospital will have a recovery division which will not only be equipped with every resuscitative measure but will also have the trained personnel. In the immediate postoperative period we do not need special nursing, but we need specialized nursing.

In addition to the surgical advances which have been made, a great deal has been accomplished by means of irradiation. You have heard a great deal about the million volt x-ray machines which now are available, but as yet insufficient data are available to evaluate the results obtained from their use. You have heard a great deal about the so-called "atomic cocktail." Unfortunately, there are not many cases in which the radioactive isotopes are of therapeutic value, because of the lack of selective absorption by various tissues of radioactive substances. Cancer of the thyroid is the one type of cancer which may be amenable to radioactive isotope therapy. Thyroid cancer which is actively functioning can be treated satisfactorily with radioactive iodine because the thyroid absorbs iodine selectively. Unfortunately, however, too frequently the cancerous portion of the thyroid does not function as thyroid and therefore does not absorb the radioactive iodine.

The greatest use for radioactive isotopes is the study of cancer and normal growth processes. A great deal is being accomplished at present under the research program of the American Cancer Society by the use of the radioactive isotopes. I believe the time will come when we will know enough about the growth of cancer cells generally to be able to accomplish the same thing in the treatment of cancer as has been done in the treatment of infection.

As many of you know, antibiotics and chemotherapeutic agents are effective against infections because they interfere with the growth of bacteria. The sulfonamides do not kill bacteria but they simply interfere with the nutrition of bacteria so that the normal resistance of the body can overcome them. It is likely that the ultimate cure of disseminated cancer will be accomplished in the same way. We must determine what are the essential elements necessary for the growth of the abnormal cells and then it probably will be relatively simple to use a substance or substances which will interfere with the utilization of these essential elements by cancer cells.

In order to accomplish this it is necessary to understand the fundamental biologic processes necessary for cell growth. In order to put the research program on a sound scientific basis, the American Cancer Society when it set up its research program turned to the National Research Council, which is the branch of the federal government which is concerned with scientific investigation, and asked it to set up an organization to evaluate the various research projects. As most of you know, the National Research Council established the Committee on Growth, not the Committee on New Growth or not the Committee on Cancer but the Committee on Growth. It is logical that before we know what is the cause and the reason for the growth of abnormal cells we must understand the reason for the growth of normal cells. In order to carry on the research program, 25 per cent of all the funds collected by the American Cancer Society is allocated to research. The applications for funds for research are screened and evaluated by the Committee on Growth of the National Research Council and in this way you can be assured that your money, the money which you are collecting in the name of the American Cancer Society, is being used wisely in helping solve the cause of cancer.

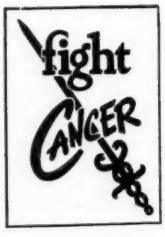
In addition to the results which are being obtained by surgery and irradiation much has been accomplished within recent years by other methods. We heard this morning about the results obtained by the use of hormones. It does not take a great deal of imagination to envisage in the relatively near future that a great deal more can be accomplished by the use of these substances. By the use of the male or female hormones, palliation and at times almost a cure can be obtained. We heard today about patients with cancer of the prostate treated by hormones for as long as 10 years without any evidence of recurrence. This is one type of cancer which

is particularly amenable to the use of hormones.

With the introduction of the research program of the American Cancer Society there have been developed a large number of chemical agents which exert anti-carcinogenic effects. These are being used extensively and intensively in the research program. Unfortunately, at the present time none of them apparently are curative, but it is astounding what can be accomplished in a palliative way. For instance acute leukemia, which previously was a uniformly fatal disease within a very short period of time, now has responded, at least in a palliative way, to some anti-folic acid substances. There are a myriad of these substances being introduced.

How long it will be before we know enough about the biologic processes to be able to interrupt the process at the particular point where normal cell growth transforms into abnormal growth, one cannot say. But it is not going to be a simple process. We know what it took to develop the atomic bomb, but this was comparatively simple. Although it required a great deal of money, manpower and time, the physicists were able to predict its completion according to mathematical formulas. On the other hand finding the cause and cure of cancer will not be simple because we are dealing with a biologic process which is much more difficult and less predictable since the living cell does not always react according to a mathematical formula. But that does not mean that it cannot be accomplished. It may require 10 years, 15 years, or even 50 years, but it is a goal worth fighting for, and I hope the time will come when we in the American Cancer Society will collect not the 13½ million that we did last year but many times that figure in order that we will have millions of dollars available for research because it is only through research that we are going to conquer cancer.

The American Cancer Society has been very wise, it seems to me, that instead of using its funds for the care of patients, its activities have consisted almost entirely of education and research. It would be entirely impossible for us to collect enough money to care for all the cancer patients. The American Cancer Society is spending its money on a continued educational program for both the laity and the professionals, and for research; and it is through these two methods that we are going to do the most to stop this scourge. Education is a very important part of our program because unless patients are aware of the importance of cancer and unless they go to their physicians for examination their early cancer cannot be detected nor can it be treated. The other attack, research, is a slower and more laborious one but ultimately offers the real solution.



Malignant Lesions of the Small Intestine

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The rare occurrence of malignant lesions in the small intestine in relation to other segments of the alimentary tract, when the small intestine comprises over two-thirds of the length of the alimentary system, is an excellent example of the capricious behavior of cancer. No satisfactory theory has been advanced to explain the rarity of neoplasms in this segment of the intestine. Neoplasms arising in "fetal rests" should certainly be as frequent in the small intestine as in other areas.

The wide range of pH values of the intestinal contents which bathe the mucosa of the duodenum, where acid gastric secretions, alkaline bile and pancreatic juice merge, might be expected to produce a certain amount of chemical trauma of this area. Yet the pylorus remains a distinct boundary between the relatively frequent carcinoma of the gastric antrum and the rare primary duodenal neoplasm.

The absence of abrupt change in the character of the mucosa has been suggested as a factor in the low incidence of small intestinal neoplasms, but such changes are not found in the stomach or colon near the site of predilection of carcinoma of these organs. The uniform fluid character of the small intestinal contents would hardly seem adequate to explain the difference in the incidence of carcinoma here and elsewhere in the alimentary tract.

Despite any adequate explanation, malignant neoplasms of the small intestine comprise only 4.9 per cent of all malignant tumors of the gastrointestinal tract.[1]

In the past, these lesions usually have been found unexpectedly at operation or at autopsy. The correct preoperative or antemortem diagnosis has infrequently been made. The difficulties in diagnosing the condition correctly are two: (1) The symptoms are usually vague and indefinite. When extensive local spread or distant metastases occur, the diagnosis may be confused by symptoms arising in other organs. (2) The condition is either purposely or inadvertently overlooked because of its rarity.

With the increasing awareness of both the general public and the members of the medical profession of the signs and symptoms of early carcinoma and the more frequent use of exploratory laparotomy (since the gradual development of safer procedures in this method), it would seem that the lesion will be encountered by the surgeon more frequently. This discussion is presented to encourage the consideration of the lesion in the differential diagnosis of obscure gastro-intestinal symptoms.

Pathology

Malignant lesions of the small intestine are usually of one of three varieties: (1) adenocarcinoma, (2) sarcoma, or (3) carcinoid.

In most of the reported series adenocarcinoma has been the most frequently encountered malignant lesion of the small intestine. In a series of cases recently analyzed by Adams and Lloyd[2] from the Wadsworth General Hospital, Los Angeles, adenocarcinoma was found six times as frequently as sarcoma. Maxwell, Crile and Dinsmore[3] reported that, in the cases seen at the Cleveland Clinic, there were 21 carcinomas, 14 sarcomas, and six carcinoid tumors. All series agree that in the duodenum, carcinoma is the most frequently encountered lesion, and it is usually the most common lesion of the jejunum. Sarcomas of the ileum have outnumbered carcinomas in some series.

Sarcomas are usually either lymphosarcomas or leiomyosarcomas. The lymphosarcomas occur most frequently in the terminal ileum. There were three sarcomas in the series of Adams and Lloyd,[2] all arising in the jejunum. Two were lymphoid in type; one was a leiomyosarcoma. Maxwell et al.,[3] state that sarcomas of the small intestine tend to grow outward from the serosa; therefore, stenosis of the lumen is a rare and late complication. Symptoms of obstruction may occur from pressure of the mass or kinking of the bowel.

Carcinoid tumors are differentiated from the other lesions of the small intestine by their characteristic histological appearance and the black granules in the cell cytoplasm when stained with ammoniacal silver salts. The neoplasm is thought to arise from the Kultschitzky cells in the crypts of Lieberkuehn and is found most commonly in the appendix. Appendiceal carcinoids are rarely malignant. Those in the small intestine, however, frequently exhibit malignant characteristics.

In a recent review of carcinoid tumors of the small intestine, Grimes and Bell[4] found that these

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Reviewed by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions of the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

tumors most frequently occur in the terminal ileum. Their predominant spread is regional, but wide-spread abdominal or distant metastases may occur.

These authors believe the appendiceal lesions produce symptoms early and are usually discovered before malignant spread has occurred. The lesions in the small intestine, on the other hand, are discovered late in their course and local spread or distant metastasis frequently occurs.

Incidence

The average age of the patients in the Wadsworth series was 53. The youngest was 39 and the oldest 73. This agrees quite well with the average age of 52.6 reported by C. W. Mayo[5] on a series of 108 malignant tumors of the small intestine. He noted that lymphosarcoma occurred more frequently in the third and fourth decades, and carcinoma, in the fourth and fifth decades.

The jejunum is the most frequent site of these malignant lesions. Adams and Lloyd[2] report seven duodenal lesions, eleven jejunal lesions, and four ileal lesions.

Primary carcinomas of the ampulla of Vater are not included in this discussion.

Family History

Adams and Lloyd[2] found a family history of carcinoma in 10 of their 22 cases and a family history of gastric carcinoma in six, or 27 per cent. The mother and sister of one patient in their series died of gastric carcinoma. This percentage even in this small series of cases is impressive. It would suggest that, in a region as "resistant" to the development of carcinoma as the small intestine, the "familial factor" may be more important than in other more commonly occurring neoplasms. This point should be stressed when taking the history of the patient with vague abdominal symptoms, and it may be an aid in the diagnosis.

Symptoms

The wide variations in the site of these lesions and in their mechanism of interfering with normal physiology produce a variety of symptoms. The complaints are usually localized in the gastro-intestinal tract. However, distant metastases may at times produce more dominant symptoms than the initial lesion. For instance, in one case from the Wadsworth Hospital series the only symptoms were those related to cerebral metastasis.

Loss of weight has been the most consistent finding in various series of cases. Weinberger and Paltauf[6] reported weight loss in 11 of 13 patients. In Adams' and Lloyd's series of cases[2] the average weight loss was 30 pounds. One patient had lost 60 pounds in weight. They remark that the degree of weight loss is out of proportion to the degree of intestinal obstruction observed. McDougal[7] and Mayo[5] have suggested faulty absorption from the intestinal tract as being a factor in the weight loss, in addition to the mechanical abnormalities produced by the tumor. Marked loss of weight does not necessarily indicate wide-spread carcinomatosis.

Abdominal pain or discomfort is usually reported to occur in about three-fourths of the patients. In the earlier lesions the pain is not severe but is described as a vague recurring discomfort most frequently located in the epigastrium.

Signs of acute obstruction, such as severe colicky pains, vomiting and distension may at times be mistaken for the initial symptoms of the disease. Careful questioning in such cases, however, will frequently reveal previous symptoms of mild abdominal discomfort and weight loss of several months' duration, which have been overlooked in the face of the severe symptoms of the acute attack.

Various authors have mentioned aggravation of the abdominal discomfort after eating, followed by relief after vomiting or gradual recession of the pain and recurrence with the next meal. The pain associated with lesions in the duodenum may be relieved by alkalies. Nausea and vomiting occur in about one-third of the cases. Hematemesis, diarrhea, or the presence of an abdominal mass may be included in the patient's complaints.

Doub and Jones[8] have attempted to classify duodenal lesions according to their position. If the lesion is located proximal to the ampulla of Vater, the symptoms are those of pyloric obstruction. These lesions occurring in the region of the ampulla produce jaundice, and lesions distal to the ampullary region result in obstruction accompanied by bile vomitus. Dixon[9] and his associates believe the prognosis is more favorable in lesions in the duodenum than elsewhere in the small intestine, as symptoms are produced earlier in the course of the disease. In Maxwell's[3] series the average time before the patient submitted to operation was two months for duodenal carcinoma, eight months for jejunal carcinoma, and 12 months for carcinoma of the ileum.

Physical Examination

Positive findings upon physical examination are variable. Evidence of weight loss is frequently observed. An abdominal tumor mass is palpable in about 15 per cent of the cases, and the mucous membranes may be pale if anemia is marked. The abnormal physical findings in all but the advanced cases are frequently insignificant. The history of the patient's illness is usually of greater aid than any other part of the examination in establishing the correct diagnosis.

Laboratory Examinations

An anemia was found in all of the cases reported by Adams and Lloyd.[2] In 43 per cent the anemia was of moderate degree, the red cell count being approximately four million, and the hemoglobin about 80 per cent. In 29 per cent, the red cell count was between three and four million and the hemoglobin varied from 55 to 89 per cent. Severe anemia was present in three cases. The average red blood cell count in their series was 3,600,000, and the average hemoglobin value was 68 per cent. Cases in which the anemia had been treated with iron, liver or folic acid prior to the establishment of the correct diagnosis had failed to respond. In four of their cases, tarry stools were reported, and in three others, occult blood was found in the stools.

Roentgenographic study of the small intestine for the diagnosis of malignant lesions has been unsatisfactory. Thin barium administered orally in small amounts in serial fluoroscopic or roentgenographic studies may demonstrate a constant defect. Maxwell,[3] et al., consider that one-half of the cases can be diagnosed with careful roentgenographic technique. However, in the various series of cases reported in the past, roentgenography has been of limited value.

Schatzki[10] recommends the introduction of a nasal tube into the duodenum and the continuous injection of a thin barium mixture as a special technique to demonstrate lesions of the small intestine. Golden[11] has pointed out that the defect in the lumen of the bowel produced by a neoplasm is usually short, four to six centimeters in length, while that produced by an inflammatory process usually involves a much longer segment of the intestine.

Differential Diagnosis

In the report of Maxwell, Crile and Dinsmore,[3] the erroneous clinical diagnoses included intestinal obstruction, duodenal ulcer, diverticulitis, pancreatitis, salpingitis and carcinoma of the stomach, pancreas and rectosigmoid.

Treatment

Resection of the involved segment of intestine and of a wedge of mesentery is the preferred treatment. Grimes and Bell[4] recommend this type of resection for carcinoid neoplasms when distant metastases are known to be present. If the tumor is fixed by local invasion or if widespread distant metastases are present, some type of anastomosis to by-pass the obstruction may be indicated, such as a gastro-enterostomy or entero-enterostomy. Unfortunately, the chief lymph node barrier for lesions of the small intestine, with the exception of the terminal ileum, lies at the root of the mesentery. Metastases to these nodes intimately involve the main trunk of the superior mesenteric vessels and preclude resection. The small intestine lacks the well developed secondary chain of lymph nodes found in the periphery of the large bowel mesentery.

Postoperative irradiation may be indicated in cases of lymphosarcoma. It is of no value in cases of carcinoma or carcinoid.

Results

Primarily because of late diagnosis, the results of the treatment of malignant lesions of the small intestine have been poor. The prognosis of the carcinoid tumors is the most favorable. Grimes and Bell[4] report an average survival time of 8.5 years following wide resection of tumors of this type and associated mesentery.

The operative mortality has varied from 60 per cent to 10 per cent. Attempts to remove large tumors which have local spread of the neoplasm into adjacent organs have been responsible, in many instances, for the high mortality rate.

In the cases of Adams and Lloyd, 16 patients were operated upon. In 11, a curative resection was attempted; in five cases various types of palliative procedures were performed. In the 11 cases submitted to curative resection, there was one postoperative death. Of the 10 patients who survived the immediate postoperative period, three subsequently died of recurrence in from eight to 18 months. Seven patients have survived from four months to eight years. One of these patients now has evidence of recurrence.

Conclusions

Malignant tumors of the small intestine are rare. They produce an extremely variable symptomatology. It is frequently late in the course of the disease before a definite diagnosis is made. Treatment is surgical excision, although in the past the operative mortality has been high and the percentage of patients surviving operation five years has been less than 10 per cent.

Earlier diagnosis is, of course, the only method of improving these results. A middle-aged patient with a familial cancer history, vague abdominal complaints and loss of weight should be carefully studied for evidence of a small intestinal neoplasm. After careful consideration, exploratory laparotomy at times will be indicated where strong suspicion of a malignant tumor exists, even though definite evidence of the lesion is lacking.

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Radiological End Results in the Control of Cancer

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The cure of cancer is not difficult, if the lesion is detected in an early stage and especially if it is accessible. Cure may be achieved by destructive methods of many types, surgical, radiological and otherwise. Surgical and radiological methods are today keenly competitive in the treatment of some small lesions, for example those of the lip, the tongue and the larynx. In the cure of other tumors, surgical and radiological methods are complementary, for example in cancer of the maxillary antrum or the corpus uteri. In perhaps a majority of lesions they are best used to the exclusion of each other; for example, surgery, not radiation, for tumors of the rectosigmoid; radiation therapy, not surgery, for cancer of the cervix.

What are the current end results in cancer control, using radiological methods as the principal or primary weapon? What are the results in the palliation of advanced cancer by irradiation? We shall attempt to answer these questions on the basis of a personal experience of some 23 years in clinical radiation therapy.

Method of Treatment

The choice of surgery or irradiation as the primary method of treatment depends upon several factors, such as the type and location of the tumor, the condition of the patient, and the availability of a competent specialist. Some physicians and many patients have an understandable feeling that "It is better to cut the tumor out." However, a moment's reflection on the number of local and distant recurrences following the most radical of surgery makes one realize that total excision of many tumors is not possible. Similarly, total destruction by irradiation is not always possible. However, irradiation is preferable in the treatment of certain lesions for the following reasons:

1. Superior cosmetic results. This is especially true in cancer of the skin of the face, about the eyelids, cancer of the lip, etc.

2. Superior functional results. This is true of the tongue, larynx and some other sites.

3. Superior clinical results. This is true in most cases of cancer of the cervix, in Hodgkin's disease, lymphosarcoma, medulloblastoma and a few other tumors.

Having decided on the method of treatment, it is important also to decide whether one's attempt is to cure or merely to palliate. If it is to cure, one must often be just as radical in irradiation therapy as one is in the surgery of cancer. The complications of adequate irradiation therapy are not negligible; nor are the complications or surgery. However, by vigilance and by judicious dosage, radiation ulcers and necrosis of cartilage or bone can usually be avoided.

The following four tables illustrate our policy on the Stanford University Service at the San Francisco Hospital. This policy has been evolved in cooperation with the surgical and pathological divisions, and represents our general plan. However, in individual cases, circumstances may require departure from this policy, and it is not suggested that it is rigidly followed in 100 per cent of instances.

TABLE I

Surgery Usually the Treatment of Choice

Accessible Sites:

1. Breast (Stage I)
2. Metastatic cervical nodes
3. Corpus uteri (Operable)
4. Salivary glands
5. Thyroid

Inaccessible Sites: (Tumor Operable)

1. Brain and spinal cord
2. Esophagus and stomach
3. Small intestine
4. Colon and rectum
5. Kidney
6. Bladder
7. Prostate
8. Lung, etc.

TABLE II

Radiation A Useful Adjunct to Surgery

1. Breast (Stage II) postoperative
2. Thyroid, postoperative
3. Uterus, corpus, preoperative
4. Ovary, postoperative
5. Testis, postoperative
6. Bladder
7. Kidney (bulky adenocarcinoma and Wilms' tumor)
8. Miscellaneous tumors, including postoperative recurrence, incomplete removal, etc. (e.g. breast, brain, skin, etc.)

TABLE III

Radiation Therapy The Treatment of Choice

Accessible Sites:

1. Skin
2. Lip and mouth, including tongue
3. Breast (Stage III)
4. Cervix uteri
5. Anal and urethral orifices

Inaccessible Sites:

1. Embryonal tumors—kidneys, testis, ovary
2. Endotheliomas—Ewing's, etc.
3. Medulloblastoma
4. Cancer of the larynx and nasopharynx—
5. Cancer inoperable, e.g. lung, esophagus, etc.
6. Cancer metastatic, esp. in bone, skin, etc.
7. Lymphoblastoma (Hodgkin's disease and lymphosarcoma) and leukemia.

TABLE IV

Radiation Therapy Rarely Indicated

1. Osteogenic sarcoma
2. Miscellaneous "adult" sarcomas
3. Cancer of the intestines
4. Cancer of the gallbladder
5. Cancer of the liver
6. Cancer of the pancreas
7. Advanced cancer with cachexia
8. Acute leukemia
9. Melanoma

Results Obtainable

The actual results obtained in a group of patients treated chiefly with radiology will now be considered. The data are usually those of five-year arrests. In some instances they will merely be five-year survivals (that is, some of the patients will have disease). In a few instances they will be 10- and 15-year results. We have a group of 50 patients with cancers in various sites whom we have treated more than 15 years ago and who are still living and well. Patients in this group are used for demonstration at our consultative tumor board meetings and are a source of inspiration to physicians in training, as well as to those skeptical of cure by radiation methods. It has been our personal experience that internists are amongst the most skeptical, perhaps owing to the large proportion of terminal or recurrent cases of cancer which they are called upon to see in their practices.

Accessible Group

Most cancers of the skin can be permanently cured by adequate irradiation. This usually means a dose of from 3,000 to 6,000 r, measured in the tumor, delivered in a period of from one to 20 days. Protraction is necessary when the tumor is large, or situated in parts such as the upper lip which are apt to be exposed to irritation or sunlight in years to come.

Squamous cell cancers on the dorsum of the hand or the sole of the foot are rarely treated; the blood supply in these areas is not sufficiently good to warrant vigorous irradiation, and we believe that surgical removal is preferable.

The reasons for failure in some skin tumors include inadequate dosage, inadequate size of field and large tumor. It is important that basal cell and squamous cell lesions be distinguished as far as possible, since the incidence of lymph node metastasis is so much higher in the squamous cell group. We no longer make any significant difference in dosage rate as regards the two types of skin cancer.

Cancer of the Lip

We have treated 121 cases of cancer of the lower lip during the last several years. Approximately half of these were Stage I (local tumor less than three cm. diameter). About one-fourth were Stage II (tumor from three to five cm. in diameter without nodes). The remainder were Stage III or IV. Some of the cases were in elderly or feeble patients who did not complete treatment. Of the 105 cases which completed treatment, 80 per cent are alive and well after five years. There are five known deaths from cancer. One case developed necrosis of the lip eight years after treatment. There were seven recurrences; when these were marginal they were sometimes retreated, but when they were central, they were treated by excision. Eight of the cases had enlarged lymph nodes on admission and two developed them after treatment. Our policy regarding nodes is to advise suprahyoid dissection when there is a palpable node, but in the absence of palpable nodes just to observe the patient. In our experience, the incidence of metastatic nodes following successful control of the primary is not sufficiently high to warrant routine neck dissection. Further, less than one-third of the patients in which we have seen neck dissection performed and which had proven metastases, were cured by the procedure.

Cancer of the Tongue

We have treated 71 patients with cancer of the tongue, largely or exclusively with radiological methods. We used a combination of external roentgen irradiation, followed by intra-oral roentgen irradiation and, in some cases, radium implantation. As in the case of the lip, we attempted to secure a tumor dose of approximately 6,000 r in four weeks time; in some very small and radiosensitive lesions we stopped at 4,500 r in about 18 days time. These doses are estimated tumor doses.

Only 11 of our tongue cases were Stage I (tumor under three cm.). Approximately one-half of the lesions occurred in the anterior two-thirds of the tongue and one-half in the posterior one-third. Sixty cases completed treatment, and 30 of these showed primary arrest. Ten of these recurred within two years. Our five-year cure rate is approximately 20 per cent, and this exclusively for tumors in the anterior two-thirds of the tongue. We have no five-year cures in lesions involving the posterior one-third. Nevertheless, palliation was achieved in many of the latter, rendering the patient's last year or so of life much more tolerable.

It is our impression that with more competent and more vigorous irradiation we ought to reach the five-year cure rate of Paterson, which is 28 per cent. The big problem in tongue cancer is, of course, the high incidence of metastatic nodes. Fifty per cent of our patients already had metastatic nodes on admission, and 15 per cent developed them after treatment of the primary lesion. Many of these nodes are deep, and even though bilateral neck dissection is done, cure is seldom achieved. Perhaps the best results in cancer of the tongue have been obtained

by Jacobson at the Radiumhemmet; 52 per cent of 103 primary cases were cured for five years; 15 per cent of 130 cases with metastatic nodes were alive and apparently well at the end of five years.

When a patient has apparent involvement of a single node, and refuses surgery, radical irradiation is advisable. We have actually succeeded in apparently controlling such very localized node involvement in a few patients by external roentgen irradiation alone (6,000 r into the node in less than

Figure 1. Figure 1A, upper left; Figure 1-B, upper right; Figure 1-C, lower left; Figure 1-D, lower right. Cancer of the *lip*. Example of cosmetic and functional result obtainable with roentgen irradiation in this site. Biopsy showed squamous cell cancer with muscle invasion. A and B before irradiation. C and D one year after irradiation. Patient well 10 years to date. Tumor dose 5000 r in three weeks. Illustrations show case before treatment and five years after treatment. (Courtesy Am. J. Roent.)

four weeks). Martin of Dallas uses interstitial radium needles of weak strength to supplement his external roentgen therapy and has five-year arrests of 25 per cent of metastatic nodes. This is indeed a very remarkable figure.

Cancer of the Cervix

The over-all results obtainable today in properly treated cancer of the cervix average about 40 per cent. That is to say, of 100 women seen with cancer of the cervix, 40 should be alive and well at the end of five years. This relatively high curability is due to the unique nature of cervical tumors plus the fact that their location is almost ideal for radium insertion. Our policy is to give a full course of external roentgen therapy to all cases, Stages I to IV, and follow this by radium therapy. We have a preference for the so-called Stockholm method, that is, divided dosage, with a total of about 7,000 milligram hours of radium for the average case, which delivers a dose of about 5,000 gamma roentgens to a point two cm. lateral to the mid-cervical canal.

The extreme importance of careful biopsy of cervix lesions in order to be sure that the lesion is carcinoma, and of adequate placement of the radium, cannot be overstressed. We believe that pathological consultation by two or three pathologists will become increasingly necessary in this era of cytologic diagnosis. The economic problem facing the housewife with cervical cancer is indeed a large one, but it is not larger than that of the housewife who sustains a serious fracture of the neck of the femur, or who develops an active pulmonary tuberculosis process. The practising physician will greatly aid his patient by carefully explaining to the husband or family as well as to the patient the need of six to eight weeks of almost continuous treatment. This is indeed a small part of the patient's entire life and if it is devoted to adequate irradiation, will greatly enhance the opportunity of cure.

TABLE I

5-Year Clinical Cures of Certain Accessible Tumors

(Radiation Therapy)

Site	No. of Cases	%	
Ca. *Skin*	1803	88	(Paterson 1946)
Ca. *Lip*	807	65	(Ebenius 1948)
Ca. *Tongue*	465	28	(Paterson 1947)
Ca. *Cervix*	1287	37	(Heyman 1942)

Cancer of the Breast

For early operable breast tumors, including tumors with low axillary node involvement, we believe that radical removal is still the treatment of choice. If microscopic examination of the axillary nodes discloses that there is definite tumor involvement, we believe that postoperative irradiation of the axilla and supraclavicular area will give a slight increase in the number of five-year survivals. We doubt if cancer in these nodes is ever fully destroyed by external irradiation; however, we believe that it is "suppressed" in the more radiosensitive types of lesion. Patients with Stage III or inoperable cancer of the breast should be treated by roentgen irradiation alone. Recurrences and metastases may be treated by various methods, depending on the age of the patient and the symptoms produced. By and large, roentgen irradiation is the primary treatment

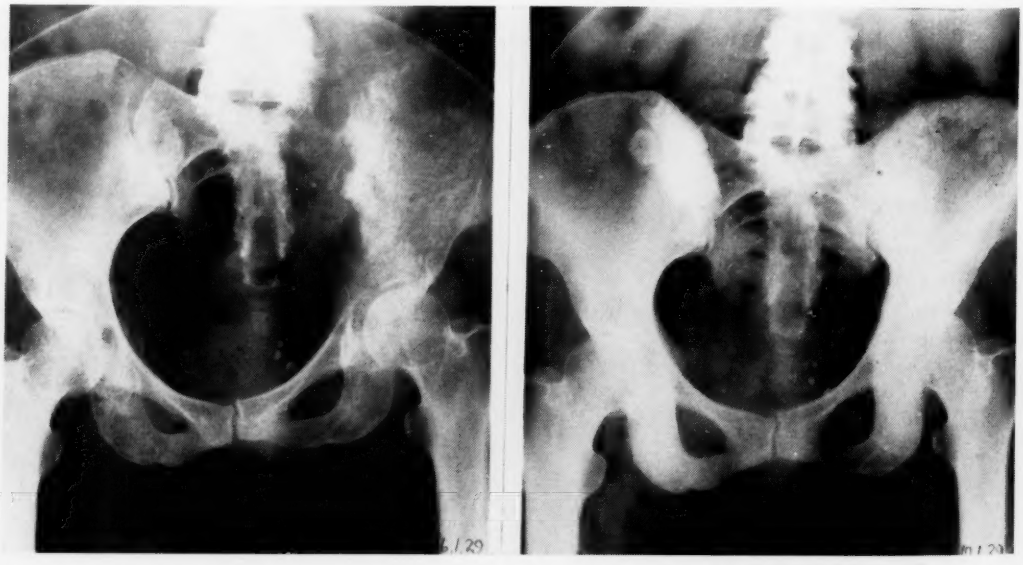

Figure 2-A, left; Figure 2-B, right. Cancer of bones of pelvis meta static from *breast.* Example of excellent palliation obtainable with irradiation: Female, age 52, with excruciating backache and left sciatic pain; breast removed one year previously for cancer. A before, and B after irradiation. Survived two years and died with liver metastases. Complete relief of symptoms. Tumor dose approximately 900 r in one week.

of choice in bone, skin and lymph node metastases. Radiation is worth using in some pulmonary and cerebral metastatic breast lesions. When metastases involve the liver we do not think radiation is worth using. If and when radiation therapy fails for the first mentioned group of metastases, then the steroidal hormones have a very useful place.

young female, plastic operation on the skin of the neck had to be performed for unsightly telangiectasis and atrophy three years after roentgen therapy. We believe that properly given roentgen irradiation is the treatment of choice for definite carcinoma of the larynx involving a single cord, and for more advanced carcinoma when there is no clinical evi-

TABLE II

Ca. Breast. Improvement in Survival with *Postoperative Irradiation.*

All Cases With Histologic Proof of Axillary Metastasis

Author	Year	No. of Cases with Radical Mastectomy Only	% 5-year Survivals	No. of Cases with Radical Mastectomy Plus Post-op. Radiation Therapy	% 5-year Survivals
Harrington	1910-1935	732	24.3	2011	29.4
Haagensen & Stout	1915-1934	154	28.2	143	36.0
Jessop	1923-1932	96	30.5	—	—
Hooper & McGraw	1918-1935	55	21.8	94	31.9
Stenstrom & Baggenstoss	1927-1941	—	—	110	41.0
	Totals	1037	25.2%	2358	30.4%

30.4 − 25.2 = 5.2%

5.2% of 25 = approx. 20% improvement with radiation.

(from Stenstrom, Acta Rad. 1947, *28*, 623)

Inaccessible Tumors

Cancer of the Larynx

We have treated 75 patients with cancer of the larynx with an over-all salvage rate of 20 per cent. We were fortunate in securing seven early cases for treatment, either because the patient had some complicating ailment such as hypertension or because he refused surgery. All seven cases are alive and well over five years; one of them is alive 15 years and two alive over 12. They have useful voices, their skins are in good shape. In one case, involving a

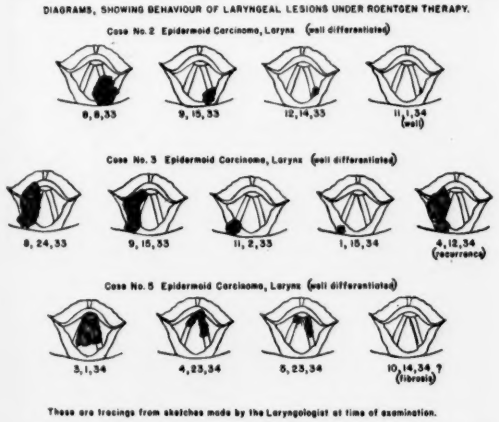
DIAGRAMS, SHOWING BEHAVIOUR OF LARYNGEAL LESIONS UNDER ROENTGEN THERAPY.
Case No. 2 Epidermoid Carcinoma, Larynx (well differentiated)
8, 8, 33
9, 15, 33
12, 14, 35
11, 1, 34 (well)
Case No. 3 Epidermoid Carcinoma, Larynx (well differentiated)
8, 24, 33
9, 15, 33
11, 2, 35
1, 15, 34
4, 12, 34 (recurrence)
Case No. 5 Epidermoid Carcinoma, Larynx (well differentiated)
3, 1, 34
4, 23, 34
8, 23, 34
10, 14, 34 ? (fibrosis)
These are tracings from sketches made by the Laryngologist at time of examination.

Figure 3. Behaviour of *laryngeal* cancer under roentgen therapy. The top row of diagrams refers to a patient treated in 1933; his laryngeal cancer remained cured for eight years, at which time he died of intercurrent disease. The second row refers to a case of extensive laryngeal cancer, which recurred following temporary control. The third row refers to a case which did well following radiation therapy, but developed some fibrosis. In early laryngeal cancer, the cure rate with roentgen therapy is high; advanced laryngeal cancer, with secondary infection, especially when cartilage is involved is probably best treated by total laryngectomy. (Courtesy, Calif. West. Med.)

dence of gross infection. However, for cases of advanced carcinoma of the larynx with obvious infection, and with probable extension into the thyroid or adjacent cartilages, it is probable that radical removal of the entire larynx is the safest and most useful procedure.

Cancer of the Lung

For inoperable cancer of the lung, properly given roentgen irradiation has much to offer. When the patient has one of the three cardinal symptoms of pain, cough or hemoptysis, a course of irradiation over the involved bronchus and the adjacent nodes will give palliation for periods of six to 24 months in a majority of cases. We have no five-year survivals in squamous cell carcinoma of the lung. It is reported that Paterson has about six per cent five-year survivals; however, it is not known whether these are squamous cell or the more benign adenocarcinomatous lesions.

Cancer of the Ovary

We have analyzed our results in a series of 79 patients with cancer of the ovary treated by surgical removal of the primary tumor and as much of the metastases as could be removed, followed by one or more courses of roentgen irradiation to the entire abdominal cavity. Only about 15 per cent of the patients survived five year; most of this small group are clinically well at the time of report, but since it is known that ovarian cancers may sometimes recur as long as 15 years after removal, one can never be sure of complete success. We believe that the work of Freed and Pendergrass has shown definite evidence of significant improvement in end results with

the addition of postoperative irradiation in cases of carcinoma of the ovary, except when the tumor is very small and has been entirely removed, together with the contralateral ovary.

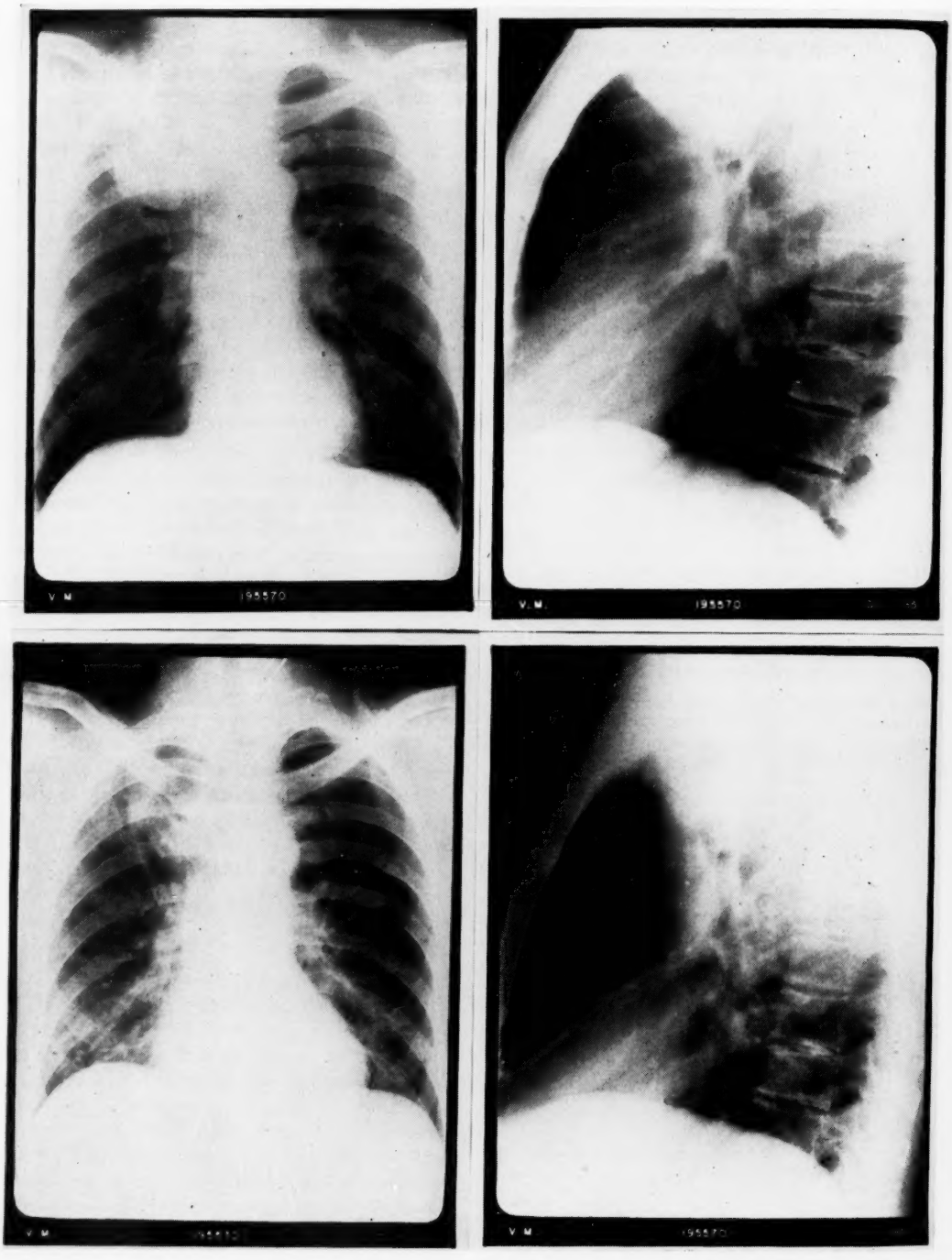

Figure 4-A, upper left; Figure 4-B, upper right; Figure 4-C, lower left; Figure 4-D, lower right. Cancer of *lung*. Example of palliative results obtainable with irradiation. Male, age 55, with cough, hemoptysis with slight chest pain: A and B before irradiation; C and D one year after irradiation. Patient relieved of symptoms for two years: then gradual recrudescence and ultimate death with cerebral metastasis. Microscopically epidermoid cancer. Tumor dose 4000 r in four weeks.

Lymphoblastoma and Leukemia

For purposes of brevity these two lesions will be considered as a group. The work of Hamann and Hodges at the University of Chicago has shown the relatively good control obtainable with properly given roentgen irradiation. Our experience with nitrogen mustard therapy has not been extensive, but is sufficient to suggest that the remissions obtainable with that chemical are of shorter duration than those obtainable with properly given and properly spaced roentgen therapy. It is generally agreed now that most cases of chronic leukemia do better with small doses of roentgen irradiation than with irradiation by internally administered radiophosphorus.

TABLE III

Results of Radiation Therapy in Lymphomas
(Survival *after* beginning of x-ray therapy)

	Cases	3 Years	5 Years
Chr. Myelog. Leukemia	49	33%	14%
Chr. Lymph. Leukemia	51	30%	23%
Hodgkin's disease	143	35%	21%
Lymphosarcoma	77	12%	9%

(*Average* survival in first three groups approx. 32 mo.*)

Figure 5-A, left; Figure 5-B, right. Cancer of *bladder*. Example of palliation which can be achieved with external roentgen therapy. Male, age 72, with hematuria. Extensive nodular tumor of right side of bladder. Biopsy showed moderately well differentiated carcinoma. Tumor dose 3200 r in four weeks in October, 1947. Bleeding stopped; follow-up cystograms in May, 1948, disclosed smooth bladder outline. Cystoscopy showed no evidence of tumor. Patient controlled for two years.

Permanency of Radiological Cure

We have investigated the permanency of radiological arrest of cancer in a group of 50 cases treated from 10 to 20 years prior to this analysis. The group comprises the usual spread of curable lesions, namely cervix uteri, corpus uteri, lip, skin, larynx, and a few miscellaneous visceral lesions. It also includes 13 cases of Stage II cancer of the breast in which arrest has been obtained by a combination of surgical and radiological means. In all instances the microscopic diagnosis made at the time of the initial roentgen therapy has been reviewed, and if necessary, the original blocks resectioned by the consulting pathologist. The series of cases is not large, but is invaluable documentary evidence of the fact that selected cancers are controllable.

Summary

In this brief outline we have emphasized that permanent cure can be obtained by radiological methods alone in suitable cases of cancer. As with surgical methods, radiological methods are most successful in the accessible group of tumors. By careful attention to this group, it is believed that the present cure rate can be doubled. It is not suggested that we should diminish our efforts at control of inaccessible tumors. However, we must be realistic as to the relative results obtainable today, and encourage the widespread use of therapeutic methods of proven value in the area wherein they are most useful.

Tumors of the Testis

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St. Louis, Missouri

It has been my privilege for the last eight years to study all the material on tumors of the testis in what was the Army Institute of Pathology and which is now the Armed Forces Institute of Pathology. To give you some idea of the magnitude and volume of that material, there were recorded in the files of that institute 1,200 examples of tumors of the testis up to December 31, 1948. Most of these were accumulated at the Institute after 1940.

I think that most people have had the experience that we have had in studying this material. By we I include a number of other individuals, particularly Dr. Nathan Friedman, who is now in Los Angeles at the Cedars of Lebanon Hospital; and Dr. Frank Dixon, who is now on the staff in the Department of Pathology, Washington University School of Medicine, St. Louis.

In the first 25 tumors of the testis which are examined microscopically, you are certain that there are 25 different kinds of tumors of the testis and that every one is a little different; but after you have studied 100 examples of this tumor you come to the conclusion that perhaps there are only 50 different kinds. After you have studied 300 or 400 you decide, or let us say that we have felt, that there are only four kinds of tumors of the testis significant in terms of histological structure and of prognosis. From the standpoint of the patient, and from the standpoint of clinical medicine, one need recognize only four types of teratoid tumor of the testis.

Now perhaps I might take a moment to explain what I mean by teratoid tumor. If you assemble together all of the tumors of the testis which are available in any laboratory, you find that somewhere between 97 and 98 per cent of those tumors fall into the class which can be termed collectively teratoid tumors. There are one per cent or two per cent of interstitial cell tumors of which I will not speak this morning, and less than one per cent of a wide variety of tumors which are not characteristic of the testis, fibromas, myomas, angiomas and other tumor types. For all intents and purposes the study of tumors of the testis is the study of the teratoid group of tumors.

Now we shall review the four types which we believe to be the basic cellular types of teratoid tumors of the testis (slide). The first is what is generally called an adult teratoma. The adult teratoma is characterized grossly as a tumor of moderate size which is firm in consistency, is sharply encapsulated and circumscribed from the surrounding testicular tissue. On cut section it is composed of gray or gray-white fibrillary tissue throughout which there are scattered tumor islands of white epithelial tissue, or yellow glandular epithelial tissue, islands of cartilage and bone, and other structures which may be recognized grossly.

Microscopically, it is composed exclusively of an adult type of tissue of varied types. Most characteristic is glandular epithelium forming a definite glandular space surrounded by a supporting tissue, and frequently about the glandular epithelium smooth muscle fibers. The adult teratoma is an organoid type of tumor in which there is an inter-relation between the various cellular types. This inter-relation is essentially that of the normal somatic structures of the body and we may recognize in these teratomas very definite structures such as stomatial epithelium, gastro-intestinal tract, respiratory tract, bronchi and various other organoid structures.

The next slide is an example of a dermoid type of structure in which there is a space lined by stratified squamous epithelium with accessory structures of the skin in the wall surrounded by connective tissue, but devoid of muscle. Muscle does not differentiate around the squamous type of epithelium. Dermoid cyst as such is an extremely rare tumor in the testis as compared with its occurrence in the ovary.

The five-year survival rate of the teratoma is about 95 per cent. Five per cent of all patients who show on microscopic examination nothing but adult structures will die within five years from metastases of a malignant tumor. I shall have more to say about this later, inasmuch as it is an extremely important point in the evaluation of the teratoid tumors of the testis.

The second type of the tumor we have chosen to call seminoma. It has also been designated embryonal carcinoma with a lymphoid stroma and has more recently been called, particularly in the ovary, a dysgerminoma. This is a type of tumor that occurs both in the testis and the ovary. It is characterized grossly as a tumor of small to moderate size (rarely of large size), which is circumscribed from the surrounding testicular tissue on gross examination but is not encapsulated. It infiltrates very slightly into the surrounding testicular tissues.

On the cut section it is gray in color, finely granular, and bulges from the cut surface. The cut surface

does not show foci of necrosis or hemorrhage which are characteristic of other types of testicular tumors. This is a fleshy gray, finely granular tumor tissue without foci or necrosis or hemorrhage.

Microscopically it is characterized by large islands of cells separated from one another completely or incompletely by connective tissue trabeculae which are infiltrated with lymphocytes, plasma cells and eosinophilic leukocytes. The individual cellular type can be seen better in the next slide in which there are prominent cell walls, and where the cytoplasm in the characteristic tumor is a clear type with very little protein in the cytoplasmic structure. The nuclei occupy one-half to one-third of the cell and have a prominent mass of chromatin or nucleolus in the center of the nucleus. The connective tissue stroma is of varying amount, infiltrated with a varying degree of cells.

After adequate treatment (and by adequate treatment I mean surgical removal of the testis and of the cord, with either x-ray radiation to the abdomen or radical removal of all of the lymph nodes as far as the renal artery), you may expect somewhere between 60 and 70 per cent of five-year survivals with this type of tumor.

The third type of tumor we have called an embryonal carcinoma. This tumor is characterized grossly as a large bulky tumor which replaces the testis, and frequently testicular tissue cannot be identified. It is soft in consistency, not encapsulated, and on the cut section consists of soft tissue with numerous foci of necrosis, hemorrhage and at times, calcification. The entire tumor is rarely if ever completely replaced by hemorrhagic tissue (which is characteristic of the fourth type that I shall discuss in a moment).

Microscopically this tumor has a varied structure, but the basic pattern is the type of cell which you see here, gathered together in lobules surrounded by connective tissue trabeculae which may be infiltrated with a few lymphocytes. The cell type is radically different from that of the cell type of the seminoma in that the cell walls are difficult to establish, and the cytoplasm has a tendency to be amphophilic; in other words, to take some degree of basophilic staining. It shows a tendency to be vacuolated, and apparently the vacuoles in the adjacent cells may become confluent to make larger vacuolated spaces. The nuclei are lightly chromatic, containing several knots of chromatin throughout the nucleus with some condensation of chromatin at the periphery of the nucleus. The foci of necrosis are prominent both grossly and microscopically such as you see in the top part of this section. The variance where there is confluence of the vacuolar spaces with the establishment of what appears to be almost a glandular or papillary type of epithelial structure is seen in this section.

Five-year survival rate after adequate therapy with the embryonal carcinoma will not exceed 30 per cent.

The fourth type is the chorio-carcinoma, the tumor identical in histological structure with the tumor occurring in the uterus after a pregnancy. This tumor is characterized by two types of cells, one of which you see here and one here. This cell is large with an indefinite cell border having a vacuolated cytoplasm with multiple nuclei of the type which I have just described as the syncytial trophoblasts of the developing placenta. It is that cell which is definitely related to the chorio-carcinoma. This cell is identical to that of the embryonal carcinoma, so far as can be determined, and represents the cytotrophoblast of the developing placenta. Now the chorio-carcinoma must have two cellular types, the cytotrophoblast and the syncytial trophoblast, in some relation to one another. That relation may be irregular such as you see in this example. In the next slide you see a regular relation between the syncytial trophoblast on the outside and the cytotrophoblast on the inside representing abortive, immature chorionic villi of a developing placenta. The cytotrophoblast is the cell that makes chorionic gonadotropins whether it be in the normally developing placenta or in the chorio-carcinoma. I shall have some more to say about that in a moment when we speak of the relation of these tumors to production of hormones and the use of the identification of those hormones in the diagnosis of the tumor types.

In chorio-carcinoma five-year survivals are either zero or something under one per cent. The five-year survival of a patient with an established diagnosis of chorio-carcinoma is a great rarity.

Now these four cellular types in contrast with most of the somatic tumors of the body are not absolute in terms that every tumor has only one cellular type. In fact, in 237 tumors, where we made 368 diagnoses, we found that on an average there are one and a half cellular types for each tumor so that most teratoid tumors of the testis are, if you wish, mixed tumors in the sense that they contain two or more cellular types. Of these 237 tumors with 368 diagnoses, we diagnosed adult teratoma 108 times, seminoma 100 times, embryonal carcinoma 144, and chorio-carcinoma 16 times. That will give you some idea of the relative incidence of these various cellular types. These are named as you can see from the discussion of the prognosis in the relative order of malignancy of the tumor.

Now these four cellular types (slides) are associated in very definite ways, for in all tumors of the group I have just described, 19 of the 108 adult teratomas were unicellular. In other words it is

relatively rare, with only 18 per cent of the tumors showing adult teratomatous structure, being purely adult teratoma. On the other hand, 71 per cent of the 100 seminomas, 26 per cent of the embryonal carcinomas, and 12 per cent of the chorio-carcinomas were unicellular. This would indicate that the seminoma, although it is a part of this group, is a little different from the others, inasmuch as it occurs much more frequently as a unicellular tumor than do the other three types of tumors. Again I shall have more to say about that later. Therefore, from the microscopic standpoint, we believe it is profitable in terms of clinical-pathologic correlation to recognize four cellular types of teratoid tumors of the testis, recognizing that these are mixed with one another in various relations in any particular tumor, and that a careful gross and microscopic study of each tumor is necessary in order to determine whether or not any one of the lower types of tumors is present, since that will materially influence the five-year survival rate.

Chorio-carcinoma and embryonal carcinoma in general are to be recognized grossly by foci of necrosis and hemorrhage so that any focus of necrosis or hemorrhage in a tumor of the testis should be carefully examined microscopically to be certain that the more malignant types are not present in that tumor.

One of the more important clinical problems in connection with tumors of the testis is that of the secretion of chorionic gonadotropin in the urine by some patients who have a tumor of the testis. This was first brought to the attention of the medical profession in the late 1920's when the statement was made that we need no longer study the microscopic appearance of a testicular tumor, but we need only determine the amount of chorionic gonadotropin in the urine and from the amount we could infer the type of testicular tumor present: small amounts, adult teratoma; large amounts, chorio-carcinoma. Many people have found that this method is not quite correct, that the problem is not as easy as that simple statement would imply.

Further study has demonstrated that in the urine of some patients with testicular tumor there are two types of gonadotropins. There is a small amount of hypophyseal, or pituitary gonadotropin, and a large amount of chorionic gonadotropin. Chorionic gonadotropin is derived from cytotrophoblasts. Further study reveals that all patients carrying testicular tumor, regardless of the cellular type, have a small amount (but excessive for the normal) of pituitary gonadotropin in the urine. Therefore in any study of this problem we must recognize two types of gonadotropin. In one instance, the pituitary gonadotropin is present in all patients with all testicular tumors, and chorionic gonadotropin is present only in certain cellular types.

It is the latter one in which I am particularly interested. Here in an embryonal carcinoma you see at the edge cells that are beginning to be multinucleated which have a distinctly basophilic cytoplasm in contrast with the other cells of the embryonal carcinoma, and if you compare that histologic structure with the developing structure of a human placenta at six or seven days of gestational period you will find that there are great similarities. This, in fact, apparently represents the early differentiation of the syncytial trophoblasts out of cytotrophoblasts, and one might conclude then that all embryonal carcinomas are in fact cytotrophoblastomas. They are tumors of cytotrophoblasts. We know in the normally developing placenta that the cytotrophoblast is the cell which makes chorionic gonadotropin. Gonadotropin is high in the early stages of pregnancy, in the first two months, and that is the time when the cytotrophoblasts begin to differentiate into fibroblasts, into angioblasts and other cells and decrease in number, and that it is at that time that there is a decreasing amount of chorionic gonadotropin in the urine of pregnant women.

The embryonal carcinoma is then a cytotrophoblastoma and this gives us support for the idea that all embryonal carcinomas should therefore have excessive gonadotropin in the urine, or all in the biologic sense of somewhere above 90 to 95 per cent. If you will check, you will find that this is true. All the embryonal carcinomas do have excessive chorionic gonadotropin in the urine.

A rare patient with a seminoma has chorionic gonadotropin in the urine, and a rare example of seminoma shows large cells that have the appearance of syncytial trophoblasts throughout the seminoid structure. The next is a higher power of this cell in which you see the typical syncytial trophoblasts; multi-nucleation, irregular cell border, vacuolation of the cytoplasm, and vascular spaces running through the cytoplasm of the cells. In terms of the normal differentiation of the cells, this would mean that these seminoma cells, although they do not ordinarily demonstrate their capacity to be a cytotrophoblast, may exhibit that capacity and differentiate into syncytial trophoblasts. The seminoma cell is then, at least potentially, a cytotrophoblast, although it does not exhibit that potentiality in but one or two per cent of all patients with that cellular type of tumor.

A summary of what we believe to be the present position in relation to the urinary secretion of hormones is as follows: all patients have a small amount, but excessive over the normal, of pituitary

gonadotropin; that almost all patients with embryonal carcinoma and chorio-carcinoma have excessive amounts of chorionic gonadotropin; and that a few patients with seminoma have excessive amounts of chorionic gonadotropin in the urine. No patient with a pure adult teratoma has any excessive amount of chorionic gonadotropin in the urine.

Now to put this in practical terms. If your laboratory is carrying out a test for gonadotropin in the usual way, such as an Aschheim-Zondek or Friedman test, and is using a very sensitive method, the pituitary gonadotropin will be picked up and positive results will be reported in every patient with a testicular tumor. If you are using a relatively nonsensitive method you will pick up only the excessive amounts of chorionic gonadotropin and will report positive reports only in some of the tumors. I believe this is the explanation for the confusion and the difference of opinion that is apparent if you read the literature on this subject. If you want to be very certain of any particular tumor type, you must use hypophysectomized rats and determine which one of the two types of gonadotropin is present, pituitary or chorionic, if you are to be certain that it is present in excessive amounts and is related to the type of the tumor present.

A third point which I would like to discuss with you very briefly is histologic, but I think of some interest in relation to the nature of these tumors, and that is the organization within the teratoid tumors. Here is a piece of the gastro-intestinal tract with mucosa, submucosal lymphoid tissue and muscularis arranged in two layers, with the blood vessels penetrating the muscularis exactly as they do in the normal intestine. The next is a higher power of the intestinal mucosa, the mucosa on the two sides, and in between lymphocytes, plasma cells and eosinophilic leukocytes in this intestinal mucosa. The point that seems to me of some interest, one which pathologists have discussed for years, is whether or not the presence of eosinophilic leukocytes in the intestinal mucosa is normal or abnormal. Here, certainly, it occurs in the intestine present in a teratoid tumor of the testis, hence the eosinophilic leukocyte must be an integral part of the normal intestinal wall, and has no relation to worms or intestinal contents that may be contained within the lumen.

Here is a joint found in one of these teratoid tumors, with two pieces of cartilage, a joint space and little villi extending into it at this side. When two pieces of cartilage come together there is an induction and change in the tissue between them and the formation of a joint.

Next is a piece of stomatial epithelium. Here is the epithelium that can well be lip, here the developing lamina of the tooth, and down here stomatial epithelium that has a close resemblance to enamel epithelium. This is a very common type of cell. The next is a higher power of this structure in which you see the enamel type of epithelium and between the epithelium and connective tissue a fine red line which is an early deposit of dentine around this enamel organ. Outside, the connective tissue cells are becoming more compact to form the odonoblasts of this developing tooth.

Next is skeletal muscle, characterized by peripheral nuclei and connective tissue in between. Next is bone with many osteoblasts along the edge and as yet no developing of the bone marrow, but the many examples of bone in these tumors will result in bone marrow within the marrow cavities.

So much for organization and induction in these teratoid tumors. The presence of one type of tissue will induce the presence of another type in some definite relation to it. I think it is fair to say that a careful study of a large series of teratoid tumors of the testis would probably tell us more about the problems of experimental embryology, the induction and organization that goes on in the formation of somatic organism, than the study of the normal development of that same organism, because you have every possibility and combination in these teratoid tumors.

Now to return for just a moment to this problem of the adult teratoma. A patient dies of the metastases of a malignant tumor. Here is the pampiniform plexus of the patient who had a teratoid tumor of the adult teratomatous type which was entirely benign. You see within the lumen of the pampiniform plexus, vascular invasion by tissue of an adult type. We can draw either one of two conclusions concerning this. First, that this tumor was always benign and that this benign tumor invaded a venous plexus. I think in terms of general pathology, that is untenable. The other explanation is that this tumor was once upon a time malignant, at which time it invaded the vascular structures, and subsequently it differentiated into a more benign adult type of tumor. This is not unknown in general pathology.

There are a number of examples in which a malignant tumor, particularly of the nervous system, has differentiated into a benign tumor over a period of months or years in which successive biopsies showed that it was originally malignant and subsequently benign. I believe that is the explanation for the occurrence of this type of tissue in vascular spaces and is the explanation for the death of five per cent of these patients with adult teratomatous tumors. That the tumor was once malignant (and I would extend that to the point that all testicular

tumors originate as malignant tumors), and that some of them differentiate itno benign tumors during the course of development of the tumor, is my belief.

Now a final point concerning histological structure, which I believe bears on the nature of these tumors. In studying many testicular tumors, you will at some time be impressed with this structure—a roughly oval or round structure in two dimensions of compacted connective tissue on the outside of a very primitive type with a very loose type of connective tissue inside. At some point one or more spaces will be lined with a flattened type of cell at one or more places, at another point an epithelial type of structure within that loose connective tissue; and at one or more places a group of syncytial and cytotrophoblasts will represent a developing placenta. Next is a variation of this in which you see the syncytial and the cytotrophoblasts, here the thin-walled space, and up here the epithelium. When I first saw the microscopic appearance of this photomicrograph, I felt certain that I had seen something in the literature like it. I turned to Arthur Hertig's papers on the early stages of the developing human embryo and there is an almost exact picture of a normal-developing, human embryo, except that the embryo in this tumor is down here under normal conditions. It is not too much to expect that an embryo developing in a malignant tumor of the testis would have the embryo slightly misplaced in relation to the amniotic cavity.

Now if there occur, and I believe they do occur, embryos in teratoid tumors of the testis, we are forced to the conclusion that the origin of these tumors is from the totipotential sex cell, and we are forced to the conclusion that the sex cell undergoes parthenogenesis. Thence, from it develop all the structures of the normally developing embryo, Heuser's membrane (the thin-walled membrane), the amniotic cavity, the embryo, the placenta, and the extracelomic mesoderm exactly as it occurs in the normally developing embryo.

Now, to try to put all of this together for you in a few minutes. Under normal conditions the sex cell undergoes fertilization. There is a fertilized ovum, and from that fertilized ovum two types of cells develop: the somatic cells, which will make the organism of the next generation, and the trophoblastic cells, which will be used as the placenta for a limited period of time and then discarded. Now if this sex cell undergoes orthogenesis, a totipotential cell could be formed in exactly the same way and from that totipotential cell there would develop trophoblastic cells and somatic cells exactly as on the normal side. This is the line of formation of all tumors of the testis from the sex cell.

If these somatic cells went on to develop into tissues that resemble the somatic cells of the child and the adult, there would be two stages: immature teratoma in which the structure would resemble very immature fetal tissue and the more mature which is the usual type where bone, muscle, gastrointestinal tract and other normal structures are seen. Under very rare conditions a carcinoma could originate in a mature teratoma. I think I have seen a few carcinomas of the testis that probably are not teratoid tumors, but represent carcinomas of the colon originating in a colon of a teratoid tumor of the adult type. But that is a very rare type of testicular tumor.

As the trophoblastic cells develop, they may develop first into cytotrophoblastoma or the embryonal carcinoma, and if there is further differentiation they go over into the chorio-carcinomas. We then have three of the four cellular types which I described: the teratoma, the embryonal carcinoma, and the choriocarcinoma. Now, remember that I submitted some evidence to you that the seminoma was a little different—not quite the same type yet it was within the group—so let us go on to the next slide in which you bring the seminoma down as a direct neoplastic proliferation of a sex cell, to put it not only within the group but also in a little different group. However, we know that the seminoma is at times associated with these other tumor types. It is not completely isolated and separate from the other three, so that in the next slide we might draw a little dotted line across to indicate that parthenogenesis within the seminoma may occur. This process is rare in comparison with the direct neoplastic proliferation and with direct pathogenesis and the development of the other tumor types. The association of the seminoma with the other tumor types you remember occurs in less than 30 per cent of all seminomas.

Now on the final slide I have placed a dotted line about those cells in the teratoid tumors and in the normally developing somatic organism which develop and excrete into the blood stream chorionic gonadotropins. The other tumor types do not develop chorionic gonadotropin in the urine. This places testicular tumors in a little different group from the other somatic tumors of the body, and they represent a tumor which is comparable to a person of the next generation, when they occur in the gonads. When they occur in other parts of the body, perhaps they represent siblings of the individual carrying them, in that a totipotential cell is left over in development along the midline, in the pineal region, in the mediastinum, or in the sacral-coccygeal region. From that totipotential cell, a sibling of the somatic organism carrying it, there develops a

teratoid tumor. But the ones in the gonads represent a tumor of the next generation.

All teratoid tumors of the testis are in one group, and there are four cellular types, these being associated with one another in a variable proportion. The determination of the amount of chorionic gonadotropin in the urine is valuable in diagnosis and prognosis, provided you determine chorionic and not chorionic and pituitary gonadotropin. This classification and theory concerning testicular tumors fits in well with clinical experience, in that the four types represent different clinical types with different prognosis and different clinical behavior.

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